

# ANNUAL REVIEW OF NUCLEAR SCIENCE

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## PREFACE

The present volume, although the third in the series, is the first for which the Editorial Committee and Editors are fully responsible. In planning this and subsequent volumes, an arbitrary and difficult decision has been made in choosing what topics should be reviewed in covering the entire field of "nuclear science." To the more or less standard topics such as nuclear reactions, structure and instrumentation it has been decided to add chapters on the interaction of nuclear radiations with chemical and biological materials and systems, the latter even including the research man himself. With such a broad concept it is not possible to cover the entire range of topics in a single volume. This is not any serious handicap since progress in some fields of activity is such that they do not warrant a review every year. Because of the resulting somewhat less than complete coverage in each volume, the reader should evaluate the *Annual Review of Nuclear Science* in terms of an integration over two or three years. The reader is encouraged, nevertheless, to comment on any volume at any time and at any length to the Editorial Committee or to the Editors.

In a review volume certain compromises must be made. Available space limits complete and detailed reporting. The desire to achieve a maximum "information density" interferes with the attainment of clarity. To inform the specialist in field "A" about the status of field "B" requires that the fields be reviewed in a manner understandable to "B" and "A" specialists, respectively. This latter, in turn, requires a somewhat broader approach than the specialist in the field might desire. It should be noted that, while individual chapters may take a broad approach, they do not take an elementary approach. If the specialist in a particular field wishes to learn of the status of another field, he must prepare himself with a minimum knowledge of the fundamentals of the new field. The fundamentals cannot be provided in a review volume such as this, although the literature cited at the end of each chapter often include useful general references. One of the goals of these volumes is to encourage specialized research men to be currently aware of progress in related fields and to dig out, not necessarily from these reviews, the basic concepts involved in research in those other fields.

In acknowledging the generous cooperation of the authors in preparing the various chapters, it should be pointed out that they are in a substantial way responsible for the pattern of the book. Until the *Annual Review of Nuclear Science* is a few years older each author will not be able to rely on precedent in shaping the general features of his chapter.

J.G.B.	D.F.M.
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# REACTIONS OF $\pi$ -MESONS WITH NUCLEONS<sup>1</sup>

By E. M. HENLEY, M. A. RUDERMAN, AND J. STEINBERGER

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The information obtained from experiments with artificially produced  $\pi$ -mesons concerns: (a) properties of the free mesons: charge, mass, spin, decay modes, mean life; (b) properties of their reactions with nucleons.

The first subject has been explored for some time, and we confine ourselves here to the briefest summary. There are three kinds of  $\pi$ -mesons: positive, negative, and neutral. The positive meson has spin zero (1, 2), and the neutral meson must have an integral spin different from one (3, 4). We will assume in the following that all three mesons have zero spin. Some of the available information on masses, decay modes, and lifetimes is contained in Table I.

A most basic result for the meson-nucleon interaction is that the parity of a  $\pi^-$  meson at rest is odd. Experiment shows that the parity of  $\pi^- + p$ , when the total momentum and the relative orbital momentum are zero, is

TABLE I  
MASSES, DECAY MODES, LIFETIMES OF  $\pi$  MESONS

	Mass in units of electron mass	Decay Mode	Lifetime	Ref.
$\pi^+$	$277.4 \pm 1.1$ (5)	$\pi^+ \rightarrow \mu^+ + (\nu)$	$(2.58 \pm .13) \times 10^{-8}$ sec.	(13)
		$> 99.9\%$ (8)	$(2.54 \pm .11) \times 10^{-8}$ sec.	(14)
	$275.1 \pm 2.5$ (6)	$\pi^+ \rightarrow e^+ + (\nu)$	$(2.53 \pm .10) \times 10^{-8}$ sec.	(15)
		$< 0.1\%$ (9)	$(2.44 \pm .18) \times 10^{-8}$ sec.	(16)
$\pi^-$	$276.1 \pm 1.3$ (5)	$\pi^- \rightarrow \mu^- + (\nu)$	$(2.55 \pm .19) \times 10^{-8}$ sec.	(16)
	$275.2 \pm 2.5$ (7)		$\pi^-/\pi^+ = 1.01 \pm .1$	(17)
$\pi^0$	$m_{\pi^-} - m_{\pi^0} =$ $10.6 \pm 2.0$ (7)	$\pi^0 \rightarrow \gamma + \gamma$ $99\%$ (4) $\pi^0 \rightarrow \gamma + e^+ + e^-$ $0.8 \pm 0.2\%$ (10, 11a, 12)	$10^{-14}$ sec.	(11a, b)

opposite to that of a stationary neutron.<sup>2</sup> The best evidence for this is the analysis of the capture of stopped negative  $\pi$ -mesons in deuterium by

<sup>1</sup> The survey of literature pertaining to this review was concluded in April, 1953.

<sup>2</sup> The  $\pi^-$  has odd parity only if  $n$  and  $p$  have the same parity. The choice is a matter of convenience. If proton and neutron had opposite parity we would call  $\pi^\pm$  a scalar and  $\pi^0$  a pseudoscalar, but there is no difference in physical content.

Panofsky, Aamodt & Hadley (7). It was pointed out by Feretti (18) that the reaction  $\pi^- + D \rightarrow n + n$  is forbidden for scalar mesons if captured into an  $S$ -state because the Pauli principle forbids a state of angular momentum one and even parity to two neutrons. Since the reaction is found to proceed with a rate comparable to that for radiative capture, the  $\pi^-$  meson must be pseudoscalar (odd parity and spin zero). We shall assume that all three  $\pi$ -mesons are pseudoscalars.

This review treats recent experimental results on the scattering and photoproduction of  $\pi$ -mesons by single nucleons. Theoretical discussions are brief and at best may serve as an orientation. Because of its importance in providing a basis for the discussion of meson-nucleon reactions the presentation of the data is preceded by a section on the implications of charge symmetry and charge independence.

#### CHARGE SYMMETRY AND INDEPENDENCE IN $\pi$ -MESON NUCLEON REACTIONS

If electromagnetic forces are neglected, then certain symmetries are possible in the way in which the three types of  $\pi$ -mesons and two types of nucleons may interact. However, charge conservation leads to essential asymmetries. For example, in the scattering of  $\pi^+$  and  $\pi^-$  mesons by protons the scattered meson can be different in kind from the incident one for  $\pi^-$  but not for  $\pi^+$  scattering.

Nevertheless, there is a variety of situations for which the restrictions of charge conservation enter in a symmetric way. For these it is attractive to introduce the hypothesis of charge symmetry: except for interactions with electromagnetic fields, a system of  $\pi^-$  mesons and nucleons is physically equivalent to another in which (a) protons are interchanged with neutrons and (b) positive mesons are interchanged with negative mesons.

The most convincing evidence for charge symmetry is the apparent equality of the low-energy  $n$ - $n$  and  $p$ - $p$  interactions. Mirror nuclei  $\text{H}^3$ - $\text{He}^3$ ,  $\text{Li}^7$ - $\text{Be}^7$ , etc., differ only by the exchange of all  $p$ - $p$  and  $n$ - $n$  interactions. Except for differences in Coulomb energy which can be estimated theoretically, any difference in the level structure of two mirror nuclei would reflect a failure of charge symmetry. Figure 1 shows the known level structures for  $\text{Li}^7$ - $\text{Be}^7$  (19), relative to their ground states. The discrepancies between corresponding levels are within the uncertainties in the Coulomb energy.

There is much corroborative evidence for the equivalence of low energy  $p$ - $p$  and  $n$ - $n$  forces (20, 21). No convincing demonstration exists at high energies below meson production threshold, but there are some experimental tests for charge symmetry in meson reactions.

The scattering of  $\pi^\pm$  mesons by deuterium has been measured at 60 Mev by Isaacs, Sachs, & Steinberger (22), and by Anderson *et al.* (23) between 70 and 130 Mev. Both groups observe the relative attenuation of  $\pi^+$  and  $\pi^-$  for  $\text{H}_2\text{O}$  and  $\text{D}_2\text{O}$ . Comparing with the  $\text{H}_2$  cross sections, they find



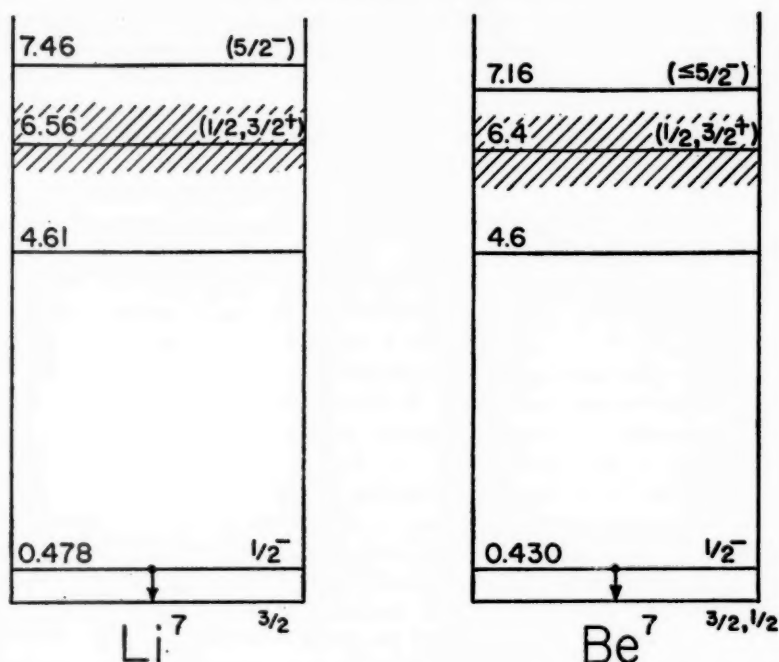


FIG. 1. States of the mirror nuclei  $\text{Li}^7$  and  $\text{Be}^7$  (19). The ground state energies are taken as zero for both nuclei. Energies are given in Mev.

the results of Table II. These results suggest the validity of charge symmetry for meson reactions, but the large errors could mask a substantial deviation.

In addition, Wilson & Barkas (24) have investigated the  $\pi^+/\pi^-$  ratio from 375 Mev  $\alpha$ -particles on carbon. However, Coulomb corrections are uncertain and possibly large, so that the relation of the experimental ratio  $0.72 \pm 0.17$  to the exact charge symmetric value is unknown.

TABLE II  
CROSS SECTIONS OF  $\pi^+$  AND  $\pi^-$  MESONS IN DEUTERIUM

Energy and energy band-Mev	$\pi^+$ Cross section, mb.	$\pi^-$ Cross section, mb.	Reference
$58 \pm 10$	$38.3 \pm 3.1$	$32.8 \pm 3.1$	(22)
$72 \pm 17$	$60 \pm 9$		(23)
$79 \pm 10$	$79 \pm 15$	$54 \pm 13$	(23)
$109 \pm 15$	$109 \pm 16$	$103 \pm 10$	(23)
$127 \pm 15$	$151 \pm 21$	$129 \pm 11$	(23)
$133 \pm 9$		$128 \pm 16$	(23)

The stronger hypotheses of charge independence of nuclear forces postulates the equality of  $p$ - $p$  to  $n$ - $n$ , and also to  $n$ - $p$  forces in equivalent states allowed by the Pauli principle. If the  $\pi$ -meson is the force field in nuclear interactions, charge independence of nuclear forces imposes certain relations among the meson-nucleon interactions. These conditions, which depend on the charge of meson and nucleon, possess no unique simplicity. They can be elegantly described through the introduction of isotopic spin, but different machinery could be invented to give a formal simplicity to other interaction schemes.

Charge independence for low energy nuclear forces was first suggested (25) by the analysis of  $n$ - $p$  and  $p$ - $p$  scattering. The singlet  $n$ - $p$  effective range is  $(2.3 \pm 0.3) \times 10^{-13}$  cm. (26) compared to a  $p$ - $p$  range of about  $2.65 \times 10^{-13}$  cm. (27) The difference in scattering lengths is consistent with equal nuclear potentials and the uncertainties of the  $p$ - $p$  and  $p$ - $n$  magnetic moment interactions. Additional evidence for charge independence appears in the level structures of isobaric light nuclei with  $A = 2Z - 1$ ,  $2Z$ ,  $2Z + 1$ . Except for Coulomb corrections, the proton-rich and proton-poor isobars are expected to have the same levels. The self conjugate nucleus ( $A = 2Z$ ) is expected to have these levels also, but the Pauli principle permits additional levels for this isobar. The assignment of the parities and spins is not yet as complete as one would like, but the existing evidence for the triplets  $\text{He}^6$   $\text{Li}^6$   $\text{Be}^6$ ,  $\text{Be}^{10}$   $\text{B}^{10}$   $\text{C}^{10}$ , and  $\text{C}^{14}$   $\text{N}^{14}$   $\text{O}^{14}$  supports the charge independence hypothesis.

At high energies the comparison of  $p$ - $p$  and  $n$ - $p$  scattering is made difficult by the restrictions of the Pauli principle for  $p$ - $p$  but not  $n$ - $p$  systems. However, Feldman (28) and Jacobsohn (29) have shown the inequality

$$\frac{d\sigma_{pp}(90^\circ)}{d\sigma_{np}(90^\circ)} \leq 4$$

to be a consequence of charge independence. All experimental results presently available meet this condition.<sup>3</sup>

The predictions of charge independence for reactions involving only nucleons are explicit, but the implications for reactions involving mesons depend on additional assumptions for the meson-nucleon interaction. It is simplest to postulate that the meson-nucleon interaction is specified by the four Yukawa matrix elements.

$$(a) \ p \rightarrow n + \pi^+, \quad (b) \ n \rightarrow p + \pi^-, \quad (c) \ p \rightarrow p + \pi^0, \quad (d) \ n \rightarrow n + \pi^0 \quad 1.$$

and their inverses. Charge independence specifies a unique set of relations among (a), (b), (c), and (d). The equality of  $p$ - $p$ ,  $n$ - $p$ , and  $n$ - $n$  forces obtains if

$$(a) = (b) = \sqrt{2} (c) = -\sqrt{2} (d), \quad 2.$$

<sup>3</sup> Experimental discrepancies in  $d\sigma_{pp}(90^\circ)$  are the main source of uncertainty. The ratio is  $2.8 \pm 0.5$  with the  $d\sigma_{pp}$  measured at Berkeley (30) and  $3.8 \pm 0.6$  with that measured at Rochester (31) and Harwell (32).

a relation which holds without reference to the method of calculation. The matrix elements (equation 1) with the relations 2 constitute the charge independent or symmetric coupling meson theory. It gives a variety of predictions about meson-nucleon scattering cross sections, meson production in nucleon-nucleon collisions, and nucleon-nucleon scattering.

Assumptions other than relation 2 can also give a charge independent nuclear force. For example, instead of the Yukawa type theory defined by equation 1, one can introduce a meson-nucleon interaction consisting of the four pair theory matrix elements

$$\begin{aligned} (\alpha) \quad p \rightarrow p + (\pi^+ + \pi^-), & \quad (\beta) \quad n \rightarrow n + (\pi^+ + \pi^-), \\ (\gamma) \quad p \rightarrow p + (\pi^0 + \pi^0), & \quad (\delta) \quad n \rightarrow n + (\pi^0 + \pi^0), \end{aligned} \quad 3.$$

and their inverses. If

$$(\alpha) = (\beta) \quad \text{and} \quad (\gamma) = (\delta) \quad 4.$$

the theory gives rise not only to charge symmetric, but even to charge independent nuclear forces. This will be true for arbitrary ratio of  $\alpha$  to  $\gamma$ . There will then be no necessary relationship between the scattering of charged and neutral mesons by nucleons, in contrast to the consequences of the symmetric coupling theory.

The charge independent theory is adopted as the simplest hypothesis which can describe the observed production of single charged mesons while giving charge independent nuclear forces.

It is cumbersome to derive the predictions of the charge independent theory in the form of equation 2. To simplify the derivation of its consequences it is useful to introduce the concept of isotopic spin. It proves convenient then to consider the proton (+) and neutron (-) as two charge states of the nucleon.

A complete set of charge states for the two nucleon systems is

$$(+)_1(+)_2, \quad (-)_1(-)_2, \quad (+)_1(-)_2, \quad (-)_1(+)_2. \quad 5.$$

For  $p+p$  and  $n+n$  the charge states are unique, but the choice of charge state to describe  $n+p$  is arbitrary. A set equivalent to equation 5 is

$$(+)_1(+)_2, (-)_1(-)_2, 1/\sqrt{2} [(+)_1(-)_2 + (-)_1(+)_2], 1/\sqrt{2} [(+)_1(-)_2 - (-)_1(+)_2]. \quad 6.$$

The advantage of equation 6 is the simplicity with which one can separate those states of  $n+p$  which are also allowed for  $p+p$  and  $n+n$  by the Pauli principle. The first three charge states of equation 6, representing  $p+p$ ,  $n+n$ , and  $n+p$ , are symmetric when the charge of 1 and 2 are exchanged; the last state, also describing  $n+p$ , is antisymmetric. When  $n+p$  is in a state which the Pauli principle forbids for  $p+p$  and  $n+n$ , we adopt the convention of assigning it the antisymmetric charge state of equation 6; otherwise  $n+p$  is described by the symmetric charge state. Then charge independence of nuclear forces means that the nucleon-nucleon interaction is the same in all three symmetric charge states.

The nucleon charge states are analogous to the spin states of spin 1/2

particles which can have either spin up or spin down. Two such particles have three symmetric states (triplet) and one antisymmetric state (singlet). If two particles interact with conservation of spin angular momentum, the interaction can depend only upon the total spin quantum number, but not upon its component in a particular direction. It is this property which makes the introduction of isotopic spin so useful for the description of charge independence. In the space of (+) and (-) we can introduce  $\tau_x$ ,  $\tau_y$ ,  $\tau_z$ , operating on (+) and (-) exactly as  $\sigma_x$ ,  $\sigma_y$ ,  $\sigma_z$  operate on ( $\uparrow$ ) and ( $\downarrow$ ). The charge states of the two nucleon system are then eigenstates of the total isotopic spin  $T^2 = (T_1 + T_2)^2$  and of its  $z$  component  $T_z = T_{1z} + T_{2z}$ . The charge of a nucleon system is given by the corresponding eigenvalue of  $T_z$  plus  $1/2$  times the number of nucleons:  $Z = T_z + A/2$ . The three symmetric charge states are the triplet with isotopic spin  $T = 1$ . The singlet has  $T = 0$ . Just as in the angular momentum case, the statement of charge independence of nuclear forces, namely that the interaction should be independent of  $T_z$ , is contained in the assumption that the total isotopic spin is conserved. It is not difficult now to relate this to the meson-nucleon interactions (equation 1). Conservation of total isotopic spin in nucleon collisions holds when the isotopic angular momentum is conserved in each of the meson-nucleon interactions which give rise to the nuclear force. Since  $T = 1/2$  for the nucleon, conservation of isotopic spin in the Yukawa reactions (equation 1) allows only  $T = 0$  or  $1$  for the meson. Emission of a  $T = 0$  meson leaves the charge of a nucleon unchanged and would correspond to a theory in which only neutral mesons are coupled to nucleons. Therefore, the isotopic spin of the  $\pi$  meson is  $1$ . Charge conservation relates  $T_z = 1$  to  $\pi^+$ ,  $T_z = 0$  to  $\pi^0$  and  $T_z = -1$  to  $\pi^-$ . The assignment of  $T = 1/2$  to the nucleon,  $T = 1$  to the meson, and the conservation of isotopic spin, are equivalent to the statement of the charge independent meson theory.

A simple consequence of conservation relates  $d\sigma(p + p \rightarrow \pi^+ + D)$  to  $d\sigma(p + n \rightarrow \pi^0 + D)$ . The deuteron has isotopic spin  $0$  since it is in a state forbidden to two protons. Therefore, the final states  $\pi^+ + D$  and  $\pi^0 + D$  have total isotopic spin  $1$  and differ only in the  $z$ -component. For  $\pi^+$  production the incoming protons have  $T = 1$ ; the incident  $p + n$  which produce the  $\pi^0$  are in a mixture of  $T = 1$  and  $0$ . Since

$$(+)_1(-)_2 = 2^{-1/2} \{ [(+)_1(-)_2 + (-)_1(+)_2]/2^{1/2} + [(+)_1(-)_2 - (-)_1(+)_2]/2^{1/2} \}, \quad 7.$$

the  $p + n$  system has a 50 per cent probability for having  $T = 1$ . Therefore, [Yang, unpublished (33)]

$$d\sigma(p + n \rightarrow \pi^0 + D) = (1/2)d\sigma(p + p \rightarrow \pi^+ + D). \quad 8.$$

Other consequences of the charge independent theory, similarly derived, are (28, 34, to 40)

$$\begin{aligned} \sigma(n + p \rightarrow \pi^+ + n + n) &+ \sigma(p + \bar{p} \rightarrow \pi^+ + p + n) \\ &= 2\sigma(n + \bar{p} \rightarrow \pi^0 + n + p) + 2\sigma(p + p \rightarrow \pi^0 + p + p). \end{aligned} \quad 9.$$

(A more complicated relationship exists among the differential production cross sections.)

$$d\sigma(\pi^- + p \rightarrow \pi^0 + n) + 2d\sigma(\pi^0 + p \rightarrow \pi^0 + p) = d\sigma(\pi^+ + p \rightarrow \pi^+ + p) + d\sigma(\pi^- + p \rightarrow \pi^- + p). \quad 10.$$

$$d\sigma^{1/2}(\pi^+ + p \rightarrow \pi^+ + p) + d\sigma^{1/2}(\pi^- + p \rightarrow \pi^- + p) \geq 2d\sigma^{1/2}(\pi^- + p \rightarrow \pi^0 + n). \quad 11.$$

$$d\sigma(p + D \rightarrow \pi^+ + H^0) = 2d\sigma(p + D \rightarrow \pi^0 + He^0). \quad 12.$$

If only a given isotopic spin state  $T$  contributes to the meson scattering,

$$d\sigma(\pi^+ + p \rightarrow \pi^+ + p) : d\sigma(\pi^- + p \rightarrow \pi^- + p) : d\sigma(\pi^0 + p \rightarrow \pi^0 + n) = 9:2:1 \text{ if } T = 3/2, \text{ or } = 0:1:2 \text{ if } T = 1/2. \quad 13.$$

For a collision of a proton or neutron with a self conjugate nucleus ( $A = 2Z$ ) the average numbers  $N$  of  $\pi^+$ ,  $\pi^0$ , and  $\pi^-$  produced at a given angle are related by

$$2N_0 = N_- + N_+. \quad 14.$$

The  $N_0/(N_+ + N_-)$  ratio varies between 0.3 and 0.9 in different observations of high energy cosmic ray events.

A direct test of the charge independent theory is the experimental verification by Hildebrand (41) of the proportionality expressed in equation 8. Using the 400-100<sup>+50</sup> Mev neutron beam from the Chicago synchrocyclotron, the  $\pi^0$  production from protons is measured by polyethylene-graphite subtraction. The direction of both decay photons and the deuteron are measured with counters. The angle between the photon counters is adjusted to detect, with high probability, only photons from the decay of  $\pi^0$  mesons with  $53 \pm 8$  Mev in the center of mass system. The angle of the deuteron then specifies the  $\pi^0$  emission angle.

With these techniques Hildebrand has obtained the angular distribution but not the total cross section for the production of  $\pi^0$  mesons. His results are compared with those of Durbin, Loar & Steinberger (2) for 53 Mev  $\pi^+$  mesons in Figure 2. The remarkable similarity of the two angular distributions is strong evidence for the validity of the charge independent theory.

### MESON-NUCLEON SCATTERING

*Meson beams.*—The recent rapid progress in our experimental understanding of the meson-nucleon interaction has been made possible by the production of meson beams in several large cyclotrons in this country. The techniques at the Carnegie Institute of Technology, University of Chicago, Columbia University, and University of Rochester are similar. The internal proton beam strikes a target of a light element. Mesons are produced in roughly 1 per cent of the nuclear collisions, perhaps one meson for each 10<sup>4</sup> protons. The mesons are deflected and focused in the fringing field of the cyclotron magnet. The focusing conditions are best for negative mesons emitted roughly in the forward direction with respect to the proton beam and positive mesons emitted in the backward direction. Because of the con-

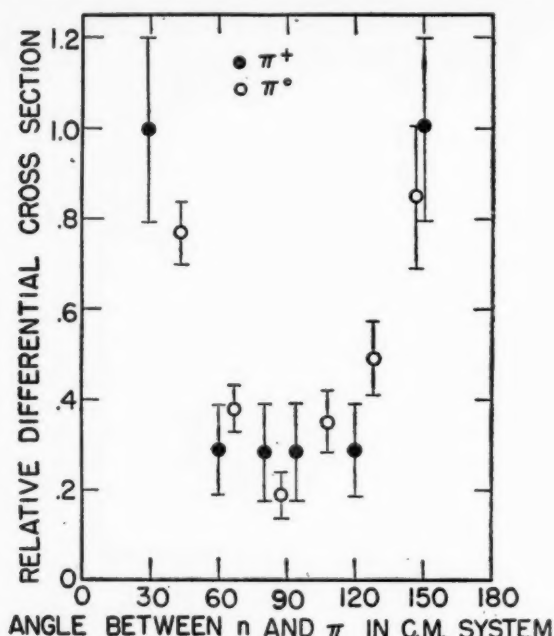


FIG. 2. Angular distributions in the center of mass system of the reactions  $p+p \rightarrow \pi^+ + D$ , ref. (2), and  $p+n \rightarrow \pi^0 + d$ , ref. (41) for 53 Mev mesons. The abscissa is the angle between the meson and the incident nucleon. The  $\pi^0$  differential cross section is arbitrarily normalized to give a best fit to the  $\pi^+$  data.

siderable velocity of the center of mass of the collision, the average energy of the backward mesons is smaller, approximately one-half that of the forward mesons. Consequently, the highest energy of positive beams with useful intensity is less than that in the negative beams. The mesons are collimated by slits in the shielding wall, which is 6 to 12 ft. thick. The slits determine the energy groups which reach the experimental area beyond the shielding. Highest beam intensities presently available are of the order of  $10^7$  mesons per hr. over an area of 4 sq. in. The energy spread is 1 to 2 per cent. At Chicago, the highest available beam energies are 220 and 140 Mev for negative and positive mesons respectively, and at Columbia 160 and 85 Mev. A lower limit of approximately 50 Mev on the energies of both positive and negative beams is set by the inability of soft mesons to escape the fringing field. In addition to the  $\pi$ -mesons, the beams contain electrons and  $\mu$ -mesons. The  $\mu$ -mesons are due to the decay of the  $\pi$ -mesons in flight. Roughly one-half of the  $\pi$ -mesons die before reaching the experimental area, which is approximately 20 ft. from the internal target. The  $\mu$ -mesons are emitted predominantly into the forward directions, and not all can be rejected in the collimating system. The usual  $\mu$ -contamination is 5 to 10 per



cent. The electrons are probably a result of the conversion in the internal target of the  $\pi^0$ -meson  $\gamma$ -rays. They have the same trajectory and therefore the same momentum as that of the mesons. Their energy is therefore appreciably higher; for example, the electrons in the 60 Mev beam must have an energy of 140 Mev. Again, the  $\gamma$ -ray, and therefore the conversion electron energies, are higher in the forward direction, so that although the electron contamination is appreciable in the low energy negative beams, perhaps up to 10 per cent, it is small in the high energy negative and in all positive beams.

*Attenuation measurements.*—The total meson cross section of hydrogen may be measured by observing the attenuation of the beam in a sample containing hydrogen. The beam, defined in a telescope of two scintillation counters, is incident on the absorber and detected in a third counter. One measures the number of mesons which disappear on insertion of the absorber. The scattering material may be liquid hydrogen, hydrogen gas under pressure, or, in a subtraction experiment, alternately carbon and polyethylene. Because of the divergence of the Coulomb scattering at small angles, it is not meaningful to perform "good geometry" measurements. The poor-ness of the geometry is chosen so that the Coulomb scattering contribution is small, but the nuclear scattering is largely included.

The method is subject to certain errors which are difficult to evaluate: (a) The beam may contain particles of insufficient energy which are detected when the hydrogen is absent, but whose range is reduced sufficiently on introduction of the hydrogen so that they escape detection. Each such event therefore simulates a nuclear process. (b) The efficiency of the final detector may depend upon the energy of the meson; it may therefore change on the introduction of the hydrogen, which reduces the beam energy. This error may be particularly large if the final detector consists of a pair of counters with absorber, because of the change in nuclear attenuation in counter and absorber with meson energy. (c) The attenuation in the carbon in the subtraction experiments, and in the container walls in the liquid hydrogen experiments, may be energy sensitive and, therefore, may be changed by the insertion of the hydrogen. (d) Recoil protons from the meson collision may be detected.

The errors become quite serious at low meson energy, partly because of the smallness of the hydrogen cross sections, and partly because of the more rapid energy variation of the cross sections of carbon, container materials, and counter materials. The presently available data should be considered preliminary. It is presented in Table III.

*Angular distribution measurements.*—The following are the main reactions initiated by charged mesons in hydrogen:

- |     |                                   |
|-----|-----------------------------------|
| (a) | $\pi^+ + p \rightarrow \pi^+ + p$ |
| (b) | $\pi^- + p \rightarrow \pi^- + p$ |
| (c) | $\pi^- + p \rightarrow \pi^0 + n$ |

TABLE III  
TOTAL CROSS SECTIONS OF  $\pi$  MESONS IN HYDROGEN AS  
MEASURED BY ATTENUATION

$\pi^-$			$\pi^+$		
Energy and Energy- spread in Mev	$\sigma$ , mb	Reference	Energy and Energy- spread in Mev	$\sigma$ , mb	Reference
$58 \pm 15$	$18 \pm 3$	(22)	$37 \pm 10$	$16 \pm 4$	(43)
$85 \pm 15$	$21 \pm 5$	(22)	$56 \pm 8$	$20 \pm 10$	(44)
$89 \pm 8$	$21 \pm 8$	(42)	$58 \pm 15$	$28 \pm 3$	(22)
$112 \pm 6$	$31 \pm 9$	(42)	$82 \pm 7$	$50 \pm 13$	(44)
$135 \pm 6$	$52 \pm 6$	(42)	$118 \pm 6$	$91 \pm 6$	(44)
$176 \pm 6$	$66 \pm 6$	(42)			
$217 \pm 6$	$60 \pm 6$	(42)	$136 \pm 6$	$152 \pm 14$	(44)

In addition, negative mesons may be captured with the emission of a neutron and a photon. This last reaction can be estimated from its inverse, the photo-production of mesons from neutrons. It contributes only a small amount ( $\sim 5$  mb) to the total cross section and will not be considered further. The angular distribution of the scattered mesons has been observed in three ways. (a) The beam traverses a diffusion cloud chamber filled with hydrogen to a pressure of the order of twenty atmospheres. The mesons scattered in the gas are observed and the event identified by the recoil proton. The charge exchange reaction appears as a meson stopping in the gas; neither of the reaction products is visible. Because of nonuniformity in the sensitivity of the chamber, no attempt has so far been made to identify such events. In one day's exposure some 5000 pictures may be obtained which contain approximately one event per millibarn of cross section and require considerable scanning effort. (b) Photographic emulsions exposed directly in the meson beam allow identification of those events which take place in the hydrogen of the emulsion by the characteristic proton recoil. Because of the low hydrogen content ( $\sim 1$  per cent) of the emulsion, scanning time is large, perhaps one week per scanner per event. Charge exchange scattering cannot be identified. (c) The mesons are scattered in a container of liquid hydrogen and the scattered mesons detected in scintillation counters. This method has several advantages; (i) The statistical accuracy is greater, of the order of 1000 events may be observed in one day; (ii) The incident beam is less contaminated by particles scattered at the apertures; (iii) Charge exchange scattering may be observed by detecting the conversion electrons of the  $\gamma$ -rays.<sup>4</sup>

In Tables IV and V the available integrated cross sections are presented. These results are considered more reliable than those of Table III because of



TABLE IV  
TOTAL CROSS SECTIONS OF  $\pi^-$  MESONS IN HYDROGEN MEASURED BY  
INTEGRATION OF ANGULAR DISTRIBUTION

Energy Mev.	$\sigma(\pi^- \rightarrow \pi^0)$ mb.	$\sigma(\pi^- \rightarrow \pi^-)$ mb.	$\sigma$ total mb.	Method	Reference
40	5 $\pm$ 1.5			Counters	(46)
53		3		Diffusion Chamber	(47)
120	21.7 $\pm$ 2.7	11.3 $\pm$ 1.6	33 $\pm$ 4	Counters	(45)
120		6.4 $\pm$ 1.7		Nuclear Emulsion	(48)
144	30.6 $\pm$ 7.5	17.0 $\pm$ 2.4	48 $\pm$ 8	Counters	(45)
135		8 $\pm$ 4		Nuclear Emulsion	(49)

\* The latter case presents the problem of inferring the neutral meson angular distribution in the center of mass system,  $\Sigma(\theta)$ , from the  $\gamma$ -ray angular distribution in the center of mass system,  $S(\theta)$ , despite the lack of complete correlation between the directions of the neutral meson and photon. Let  $W(\theta)$  be the probability of finding one of the  $\gamma$ -rays at the angle  $\theta$  with respect to the direction of motion of the decaying meson.

$$W(\theta) = \frac{(1 - \beta^2)}{2\pi(1 - \beta \cos \theta)^2}$$

where  $\beta c$  is the neutral meson velocity in the center of mass system. Then

$$S(\theta) = \int W(\theta - \theta') \Sigma(\theta') d\Omega'.$$

Following Anderson, *et al.* (45) we expand  $S(\theta)$ ,  $\Sigma(\theta)$ , and  $W(\theta)$  in Legendre polynomials:

$$\begin{aligned} S(\theta) &= \sum s_l P_l(\cos \theta) \\ \Sigma(\theta) &= \sum \sigma_l P_l(\cos \theta) \\ W(\theta) &= \sum w_l P_l(\cos \theta) \\ \omega_0 &= \frac{1}{2\pi}; \quad \omega_1 = \frac{3}{4\pi} \left( \frac{2\gamma}{\eta} - \frac{1}{\eta^2} \ln \frac{\gamma + \eta}{\gamma - \eta} \right); \\ \omega_2 &= \frac{5}{4\pi} \left( 2 + \frac{6}{\eta^2} - \frac{3\gamma}{\eta^2} \ln \frac{\gamma + \eta}{\gamma - \eta} \right) \end{aligned}$$

where  $\eta\mu c$  and  $\gamma\mu c^2$  are the momentum and total energy of the  $\pi^0$  in the center of mass system. It follows that

$$\sigma_l = \frac{2l+1}{4\pi} \frac{s_l}{\omega_l}.$$

The coefficient of a particular order in a Legendre polynomial decomposition of the outgoing scattered  $\pi^0$  intensity is equal to the corresponding coefficient in the analysis of the  $\gamma$ -ray distribution, divided by a correlation coefficient, which approaches 2 at high energies.

TABLE V  
TOTAL CROSS-SECTION OF  $\pi^+$  MESONS IN HYDROGEN MEASURED BY  
INTEGRATION OF ANGULAR DISTRIBUTION

Energy Mev.	$\sigma$ mb.	Method	Reference
43	$9 \pm 4$	Nuclear Emulsion	(50)
53	$20 \pm 5$	Diffusion Chamber	(51)
58	$15 \pm 1$	Counters	(52)
75	$41 \pm 15$	Nuclear Emulsion	(53)
78	$31 \pm 3$	Counters	(45)
110	$77 \pm 6$	Counters	(45)
135	$126 \pm 20$	Counters	(45)

the possible errors in the attenuation measurements. The tabulation of the angular distributions (Tables VI and VII) has been restricted to the counter results, chiefly obtained by the Chicago group, because of the sparseness of the data obtained by other techniques. Figure 3 illustrates the rapid rise of both positive and negative cross sections at low energy, the eventual leveling of the negative cross section, and the large ratio of positive to negative cross sections above 80 Mev.

The measured angular distributions of  $\pi^+$  mesons exhibit a large asymmetry about  $90^\circ$ , which shows that at least two angular momentum states, one even and one odd, must be prominent. For simplicity the experiments have been analyzed in terms of  $s$  and  $p$  partial waves only, although the neglect of higher order waves may not be justifiable. The number of phase shifts is further reduced by taking advantage of the probable charge independence of the meson-nucleon coupling. The six remaining phase shifts consist of  $s$ ,  $p_{3/2}$  and  $p_{1/2}$  for each of the two isotopic spin states which can be realized by the meson (isotopic spin 1) and nucleon (isotopic spin  $1/2$ ) system. Neglecting the Coulomb interaction, the cross section may be written:

$$\frac{d\sigma}{d\Omega} = \chi^2 \left\{ \left| \sum_{l=1/2}^{3/2} \beta_l \sum_{l=0}^{\infty} [(l+1)\epsilon_{l+1/2}^l + l\epsilon_{l-1/2}^l] P_l(\cos \theta) \right|^2 + \left| \sum_{l=1/2}^{3/2} \beta_l \sum_{l=0}^{\infty} \sin \theta \frac{dP_l(\cos \theta)}{d \cos \theta} (\epsilon_{l+1/2}^l - \epsilon_{l-1/2}^l) \right|^2 \right\} \quad 15.$$

Here  $\beta_{3/2}$  and  $\beta_{1/2}$  are the amplitudes for scattering in the  $T=3/2$  and  $T=1/2$  states respectively.

For

$$\begin{array}{lll} \pi^+ \rightarrow \pi^+ & \beta_{3/2} = 1 & \beta_{1/2} = 0 \\ \pi^- \rightarrow \pi^- & \beta_{3/2} = 1/3 & \beta_{1/2} = 2/3 \\ \pi^- \rightarrow \pi^0 & \beta_{3/2} = \sqrt{2}/3 & \beta_{1/2} = -\sqrt{2}/3 \\ \epsilon_{l+1/2}^t = 1/2(e^{2iL^t}_{l+1/2} - 1) \end{array}$$

$L^t_{l+1/2}$  is the phase shift in the state of orbital  $L$ , total angular momentum  $l+1/2$  and isotopic spin  $t$ .<sup>5</sup>

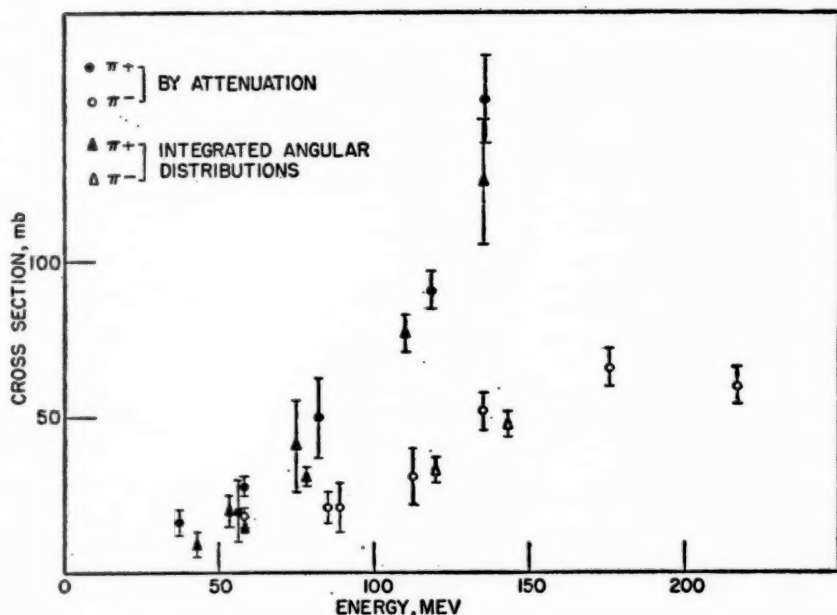


FIG. 3. Energy dependence of the total cross section for the interaction of mesons and protons (See Tables III, IV and V for references). The meson energies are given in the laboratory system.

<sup>5</sup> This may be seen in the following way. In the partial wave theory of scattering, the scattered intensity is written (see, e.g., 70a, p. 24)

$$\frac{d\sigma}{d\Omega} = \sum_{l=0}^{\infty} (2l+1) P_l(\cos \theta) \left( \frac{e^{2i\delta_l} - 1}{2} \right)^2$$

In the case of meson nucleon scattering, because of the spin of the nucleon, it is convenient to introduce the total angular momentum  $j$  which may be either  $l+\frac{1}{2}$  or  $l-\frac{1}{2}$ . Not only is  $j$  conserved, but so also is  $l$  because of parity conservation.

For a particular spin orientation of the initial nucleon, say along the direction of

TABLE VI  
SCATTERING OF POSITIVE MESONS BY HYDROGEN IN  
THE CENTER OF MASS SYSTEM

Lab. Energy, Mev.	Scattering Angle, degrees	Differential Cross Sections, <i>mb.</i>	Reference
58	36	.24 ± .11	(52)
	47	.48 ± .08	
	64	.66 ± .06	
	101	1.24 ± .07	
	129	2.10 ± .11	
	155	2.79 ± .15	
78	54	1.5 ± .25	(45)
	102	2.3 ± .3	
	143	4.3 ± .5	
110	55	3.3 ± .7	(45)
	103	5.1 ± .6	
	144	12.3 ± 1.0	
135	56	5.7 ± 2.2	(45)
	104	6.8 ± 2.1	
	145	21.6 ± 3.5	

motion of the incident meson, the incident partial wave of order  $l$  may be written in terms of wave functions with a given  $j$  and  $j_z$

$$(2l+1)P_l(\cos\theta)(\uparrow) = \psi_{l+1/2}^{1/2} + \psi_{l-1/2}^{1/2}.$$

Because of the conservation of the total angular momentum, the cross section may be written

$$d\sigma = \lambda^2 \left| \sum_{l=0}^{\infty} \sum_{j=l-1/2}^{l+1/2} \psi_j^{1/2} \frac{e^{2iL_j} - 1}{2} \right|^2 d\Omega.$$

The partial waves of given  $j$  and  $j_z$  can be analyzed in terms of waves with given  $z$  component of orbital and spin (86, p. 76)

$$\psi_{l+1/2}^{1/2} = (l+1)P_l(\cos\theta)(\uparrow) + e^{i\phi} \sin\theta \frac{\partial P_l(\cos\theta)}{\partial \cos\theta} (\downarrow)$$

$$\psi_{l-1/2}^{1/2} = lP_l(\cos\theta)(\uparrow) - e^{i\phi} \sin\theta \frac{\partial P_l(\cos\theta)}{\partial \cos\theta} (\downarrow).$$

Because of the orthogonality of the two spin functions, the resultant expression for the cross section separates into the sum of two squares as in equation 15, the first and second terms corresponding to no change in spin state, and spin flip respectively.

TABLE VII  
SCATTERING OF NEGATIVE MESONS BY HYDROGEN IN  
THE CENTER OF MASS SYSTEM

Lab Energy Mev	Angle in C.M. degrees	$d\sigma(\pi^- \rightarrow \pi^-)$ mb.	Angle in C.M. degrees	$d\sigma(\pi^- \rightarrow \gamma)$ mb.	Reference
120	55	$1.06 \pm .14$	53	$2.1 \pm .30$	(45)
	104	$.47 \pm .10$	101	$3.2 \pm .4$	
	144	$.97 \pm .18$	142	$6.0 \pm .7$	
144	56	$1.70 \pm .21$	54	$3.4 \pm .4$	(45)
	105	$.73 \pm .15$	102	$4.4 \pm .5$	
	145	$1.23 \pm .25$	143	$7.8 \pm .9$	

We have included all phase shifts in relation 15 but now restrict the discussion to  $l=0$  and 1. That is, only  $S_{1/2}^{3/2}$ ,  $S_{1/2}^{1/2}$ ,  $P_{1/2}^{3/2}$ ,  $P_{1/2}^{1/2}$ ,  $P_{3/2}^{3/2}$ , and  $P_{3/2}^{1/2}$  are taken different from zero. The angular distributions at most include terms of second order in  $\cos \theta$  and may be written

$$a + b \cos \theta + c \cos^2 \theta.$$

At each energy there are then nine coefficients, three each for the three processes, and these may be determined by measurements of the cross sections for each process at three different angles. It is then not possible, in general, to fit these nine coefficients with six phase shifts. In principle, this provides a test for the hypothesis of charge independence. Actually, the test cannot be considered critical because of the large experimental error and the neglect of higher angular momentum states. In fact, it is possible to fit the experimental data with two sets of phase shifts. These sets differ chiefly in the relative prominence of the  $P_{3/2}^{3/2}$  and  $P_{1/2}^{3/2}$  phase shifts. The best fits are presented in Table VIII. The agreement of the 120 Mev experimental points and the angular distributions corresponding to the best fit phase shifts may be seen in Figure 4. Here the angular distributions with prominent  $P_{3/2}^{3/2}$  (type A) and those with prominent  $P_{1/2}^{3/2}$  (type B) are nearly identical and are drawn as one line.

Whenever the Coulomb field may be neglected the solutions occur in pairs which differ in sign reversal only (see Table VIII). The Coulomb corrections are small for the Chicago data (45) (78, 120, 135 Mev) and were neglected. The Columbia results (52) are at lower energy, the cross sections are smaller, and the data extend to lower angles. For these reasons it was necessary to include the Coulomb effects in the phase shift reduction of the 58 Mev results. The analysis was performed according to the treatment of Van Hove (54). The solutions, A+, A-, B+, and B- of Table VIII group themselves into two pairs, one with attractive  $s$  wave and repulsive  $p$  wave interaction

TABLE VIII  
 PHASE SHIFT ANGLES

Lab. Energy Mev.	C. of M. Momen- tum in units $\mu c$	Phase Shift Angles Degrees						Type Solu- tion
		$S_{1/2}^{1/2}$	$P_{1/2}^{1/2}$	$P_{3/2}^{3/2}$	$S_{1/2}^{3/2}$	$P_{1/2}^{3/2}$	$P_{3/2}^{3/2}$	
58	.865				+ 7.4	+ 2.2	- 6.5	A+
					+ 7.4	- 9.4	- .7	B+
					- 4.9	- 1.8	+ 7.6	A-
					- 4.9	+10.7	+ 1.3	B-
78	.97				$\mp$ 6	$\pm$ 18	$\pm$ 2	B
					$\mp$ 6	$\mp$ 3	$\pm$ 13	A
120	1.24	$\pm$ 9.1	$\pm$ 3.8	$\mp$ 1.4	$\mp$ 15.4	$\pm$ 38.6	$\pm$ 12.9	B
		$\pm$ 9.0	$\mp$ 2.8	$\pm$ 1.8	$\mp$ 15.2	$\pm$ 9.0	$\mp$ 29.6	A
135	1.32	$\pm$ 10.4	$\pm$ 5.6	$\mp$ 2.9	$\mp$ 14.2	$\pm$ 49.3	$\pm$ 17.2	B
		$\pm$ 10.3	$\mp$ 4.6	$\pm$ 2.0	$\mp$ 14.0	$\mp$ 5.4	$\pm$ 37.9	A

(A+, B+) and one with repulsive  $s$  and attractive  $p$  (A-, B-). Solutions of the A type have large  $P_{3/2}$ , those of the B type large  $P_{1/2}$  phase shifts. The members of each pair (A+B+ and A-B-) exhibit the same angular distribution. However, the angular distributions of A+ and B+ differ appreciably at small angles from those of A- and B-. The results are shown in Figure 5. Whether or not the experiment discriminates between attractive and repulsive  $S^{3/2}$  state interactions depends upon the deviation which may be expected in fitting the experimental results in a theory with three free parameters. The fit with attractive  $s$  interaction ( $s_{1/2}^{3/2}$  positive) has approximately twice the expected deviation, the fit with repulsive  $s$  interaction ( $s_{1/2}^{3/2}$  negative) has approximately one half the expected deviation. The experiment therefore indicates attractive  $p$  and repulsive  $s$  interactions. Additional evidence on this point comes from the experiments on the elastic scattering of mesons in carbon. Again, observing the Coulomb interference makes it possible to fix the sign of the effective meson-nucleus potential as attractive, so that the big  $p$ -wave phase shift might be expected to be attractive.

We may then note the following features in the meson-nucleon scattering between 60 and 135 Mev, subject to large experimental uncertainties:

- All phase shifts in the isotopic spin state  $T=1/2$  are small. The state  $T=3/2$  interacts strongly.
- The largest contribution to the scattering is in one of the  $P^{3/2}$  states, but the data may be fitted equally well with large  $P_{3/2}^{3/2}$  or large  $P_{1/2}^{3/2}$ .

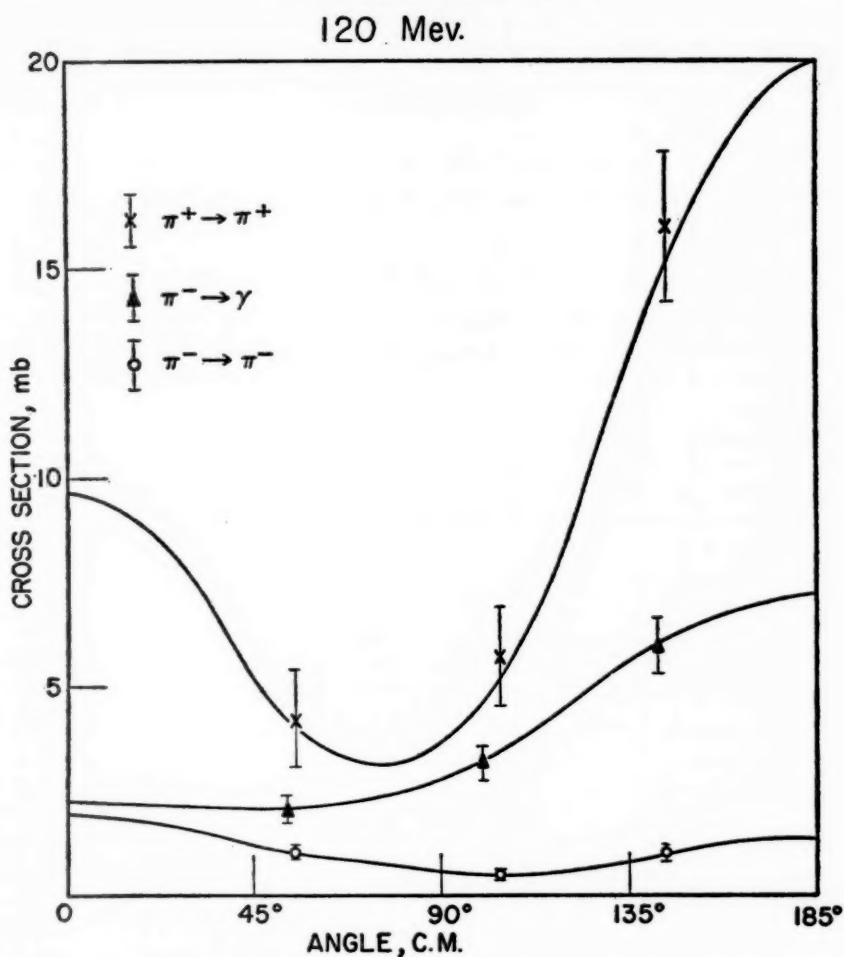


FIG. 4. Angular distribution in the center of mass system for the scattering of 120 Mev mesons by protons. The solid curves represent the angular distributions obtained with the best fit phase shifts (See Table VIII) neglecting Coulomb effects. Anderson *et al.* (45).

- (c) Both  $s$  and  $p$  wave phase shifts are roughly proportional to the cube of the momentum.
- (d) The strong  $P^{3/2}$  interaction is probably attractive, the  $S^{3/2}$  interaction repulsive.

*Theoretical descriptions.*—The experimental results on meson-nucleon scattering offer a new opportunity for investigating the validity of meson theories. It appears that the theoretical problem, although still formidable and largely unsolved, is considerably more transparent here than in the case

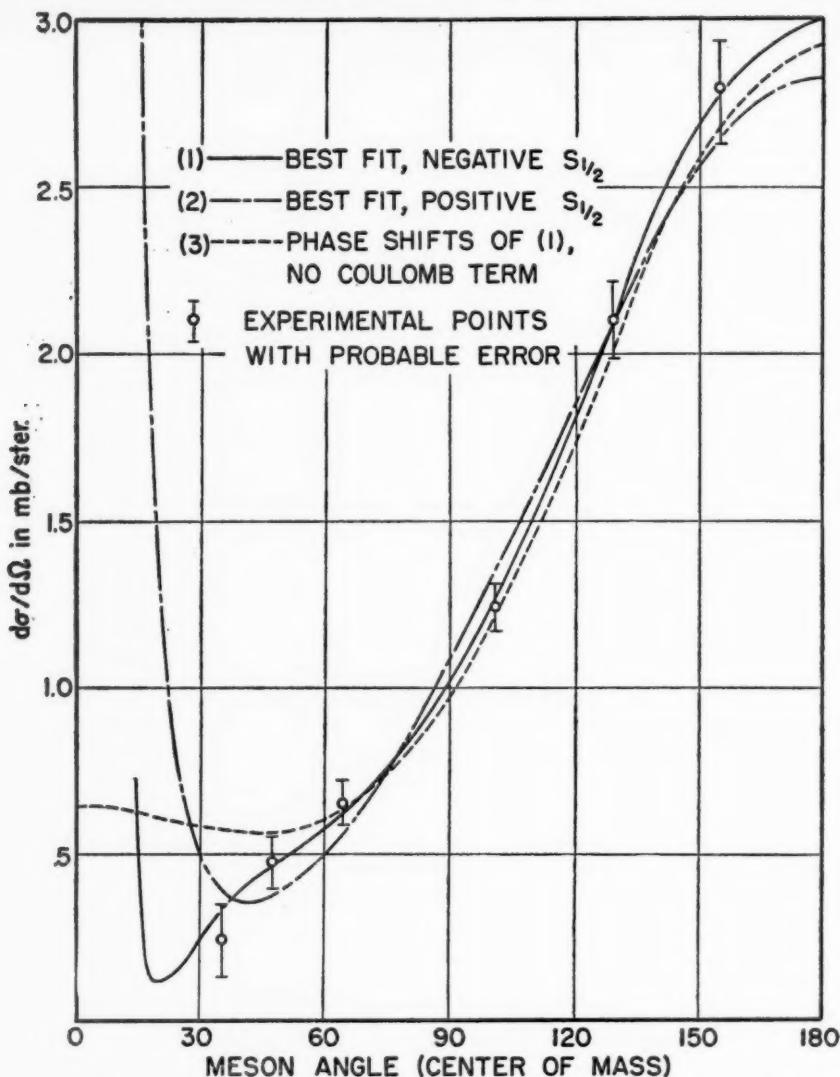


FIG. 5. Scattering 58 Mev  $\pi^+$  mesons on protons. The curves are the angular distributions corresponding to best fit phase shifts. Case (1) corresponds to attractive  $p$  and repulsive  $s$  scattering; Case (2) corresponds to repulsive  $p$  and attractive  $s$  scattering; and Case (3) corresponds to the phase shifts of (1) with the neglect of Coulomb field. Bodansky, Sachs & Steinberger (52).

of the meson theory of nuclear forces. In fact, some of the observed features of the scattering are rather simple consequences of the Yukawa theory for pseudoscalar mesons. Consider a nucleon at rest. A meson can only be emit-



ted into a state of relative orbital angular momentum 0 or 1, since the meson has spin zero. If, for the moment, nucleons in negative energy states are neglected, the parity of the nucleon does not change in this process. The meson on the other hand has odd parity, so that parity and momentum conservation require the meson-nucleon system to be in a  $p$ -state. The same considerations hold for the inverse process of absorption. If we picture the meson scattering process as an absorption and subsequent re-emission (or emission and subsequent absorption) of a meson, then in the center of mass system the scattering is expected only in  $p$ -states, except for recoil effects.

In the gradient coupling (pseudovector) theory negative energy states play only a minor role, and this result obtains. At energies considerably smaller than the meson rest energy, the theoretical energy dependence is characteristic of  $p$ -wave scattering from a short range potential: the phase shift is proportional to the cube of the momentum,  $k^3$ , and the cross section therefore to the fourth power:  $\lambda^2(k^3)^2 = k^4$ . This is a significant point of agreement with experiment, independent of detailed considerations of the model.

The dominance of the  $T=3/2$  state is theoretically not so apparent. In fact the perturbation theory does not yield this result, and although the strong coupling theory (55) predicts a large interaction in the  $T=3/2$  state, this approach seems inconsistent with the required strength of the meson-nucleon coupling.

Chew (56) has offered an intermediate and consistent approach in which the main contribution to the  $p$ -wave scattering comes from an attractive  $P_{3/2}^{3/2}$  interaction. He sums a subset of the perturbation series for meson scattering whose terms involve states with at most two mesons. This is equivalent to solving the Schroedinger equation with the interaction potential obtained from lowest order perturbation theory. This potential is attractive for  $P_{3/2}^{3/2}$  and repulsive for  $P_{3/2}^{1/2}$ ,  $P_{1/2}^{3/2}$ , and  $P_{1/2}^{1/2}$  states. The attractive phase shift is increased and the repulsive ones decreased when the scattering is calculated from the Schroedinger equation rather than by the perturbation theory, which is indifferent to the sign of the interaction. However, in addition to the strength of coupling, an arbitrary nucleon core radius must be introduced to make this approach meaningful (finite).

In addition to the type of matrix element which gives absorption and emission of  $p$ -wave mesons, the Yukawa theory permits another kind of meson-nucleon coupling. Where a hole exists a nucleon may make a transition to a negative energy state together with meson emission or absorption. Such transitions appear as the annihilation of a nucleon and antinucleon. Likewise a nucleon may jump from a negative to a positive energy state (pair creation) and emit or absorb a meson. Now the Dirac theory tells us that a particle at rest changes parity when going from a positive to a negative energy state. For example, the parity of an electron and positron in an  $s$  state (positronium) is odd. Therefore, conservation of angular momentum and parity permit the absorption and emission of  $s$ -state pseudoscalar mesons when accompanied by nucleon pair creation or annihilation. The pseudo-

scalar coupling theory has large matrix elements for precisely this kind of transition so that the perturbation theory gives predominantly  $s$ -wave, scattering. However, Wentzel (57), Drell & Henley (58), and others (59, 60, 61) have pointed out that higher order corrections should strongly reduce the  $s$ -wave phase shifts. This is because of the role of virtual nucleon pairs in the  $s$ -wave interaction. The range of interaction between  $s$ -wave mesons and nucleons is of the order of the nucleon Compton wave length, and the resultant  $s$ -wave scattering is expected to resemble that from a short range repulsion. The perturbation theory is equivalent to treating this interaction in Born approximation. It is well known that this approximation greatly overestimates the scattering from strong repulsive potentials.

In addition to the strong  $s$ -wave interaction, pseudoscalar coupling gives the same type of matrix elements as pseudovector coupling (62) and so yields the same  $p$ -wave scattering in perturbation theory. Bethe *et al.* (61) have investigated the higher order corrections with an approach similar in spirit and technique to that of Chew for  $p$ -state pseudovector coupling but with the inclusion of some of the effects of virtual nucleon pairs. Although the very large coupling constant needed with pseudoscalar coupling so far has precluded reliable quantitative calculations, appropriate choice of the coupling constant results in theoretical predictions in fair agreement with those of Chew and with experiment.

A difference in the two couplings is that the renormalization procedures, so successful in quantum electrodynamics, can be applied to the pseudoscalar but not to the pseudovector coupling theory. Therefore, with pseudoscalar coupling, it is not necessary to introduce a nucleon core, whose properties we cannot calculate, and there exists the possibility that this coupling can give a complete description of the meson-nucleon interaction.

Although the theory gives a qualitative description of the  $p$ -wave scattering, the origin of the  $s$ -wave is not clear. As we have seen,  $s$ -wave scattering of the direct coupling theory is the same as that from a repulsive short range potential; the phase shift is linear with momentum. Experimentally the energy dependence seems steeper. It is possible to devise potentials which give the experimental result (63) by adding an attractive long range tail to the repulsive core. The well parameters must be adjusted so that the  $s$ -wave is effectively cancelled at long wave lengths, whereas at short wave lengths the core predominates. Dyson (61) has pointed out that the contribution of meson-meson scattering, which has an arbitrary amplitude in the direct coupling theory, may be adjusted to yield this result.

Another interpretation of the steep  $s$ -wave energy dependence is one in which the even wave scattering is a recoil effect accompanying the  $p$ -scattering. An analysis of recoil effects in the gradient coupling theory (64) exhibits phase shifts of the right energy dependence and order of magnitude, but does not yield the proper asymmetry. A large part of the recoil scattering is found to be in the  $d$ -state.

## PHOTOPRODUCTION OF MESONS

*General.*—Investigations of the creation of mesons in nuclear collisions of  $\gamma$ -rays are in progress with the synchrotrons at Berkeley, Cornell, Massachusetts Institute of Technology (all 300 to 350 Mev), and California Institute of Technology (500 Mev) and with the 300 Mev betatron at the University of Illinois. In such machines the x-ray beam is produced by circulating electrons on striking a target of high atomic number. The angular spread of the beam is small, of the order of one half degree, and is chiefly due to the scattering of the electrons in the target. The x-ray beam exhibits the characteristic continuous *bremsstrahlung* spectrum, with roughly uniform energy per unit frequency interval up to the maximum available frequency. The beam is usually collimated in thick lead slits and monitored by means of ion chambers. The absolute calibration of the chambers in terms of the number of transmitted quanta is essential to all cross section measurements. It is a problem of some difficulty and even controversy. The first such measurement was performed at Berkeley by Blocker, Kenney & Panofsky (65); all Berkeley measurements rely on this result. Recently the calibration problem has received the attention of the Cornell group (66).

Because the x-ray spectrum is continuous, the energy of the photon responsible for a given event is generally not known. However, in photon-nucleon meson production, a measurement of any two of the four parameters of the outgoing particles, nucleon and meson momenta and angles with respect to the beam, determine the kinematics, including the energy of the responsible photon.

*Neutral photomeson production.*—Neutral photomesons were first observed by Steinberger, Panofsky, & Steller (67, 68). The meson was detected by counting its decay photons in two crystal counter telescopes. The plane of these telescopes roughly defines the angle of emission of the meson relative to the photon beam, and the angle between the two telescopes determines a most probable meson velocity. Little information was obtained on the production in hydrogen, but it was established that the excitation function near threshold is much steeper than that for  $\pi^+$  production, and that the cross section at 260 Mev is somewhat lower, but not by an order of magnitude.

Considerable experimental progress was made by Silverman & Stearns (69), who detected the recoil proton in addition to one of the  $\pi^0$  decay  $\gamma$ -rays. The proton detector was a scintillation counter sufficiently thick to stop the particle, and its energy was determined by pulse height measurement. This represents a definite advance in technique, since the correlation angle between proton and  $\gamma$ -ray is characteristic of production in hydrogen, and reduces the carbon background in these polyethylene-carbon subtraction experiments. A further improvement was a careful calibration of the efficiency of the photon detector. The results consist chiefly of four points on the excitation function at  $90^\circ$  in the laboratory (Fig. 6).

Cocconi & Silverman (70) have examined the angular distribution in experiments in which the only detected particle was one of the  $\pi^0$  decay photons. This method offers the advantage of higher yield, but does not allow a determination of the photon energy. Furthermore, the direction of the  $\gamma$ -ray only partly preserves the direction of the meson (see Footnote 5). The analysis into an angular distribution for the emitted meson was performed with the assumption that the process is entirely due to 280 Mev photons. According to the results of the excitation experiments, this is the average energy effective in  $\pi^0$  production by 310 Mev maximum energy *bremsstrahlen*. The  $\gamma$ -ray yield expected for several assumed angular distributions was computed, using the known energy dependence of the detection efficiency, and the kinematics of  $\pi^0$  decay. The experiment shows that the angular distribution is well peaked at  $90^\circ$  and symmetrical about this angle.

Probably the most elegant and extensive measurements of this process were performed by Goldschmidt-Clermont, Osborne & Scott (71). 320 Mev max. x-rays traverse a long tube filled with hydrogen to forty atmospheres at dry ice temperature. Photographic emulsions are located on the central portion of the tube, immersed in the gas, and shielded from the photon beam. Recoil protons are detected provided their angle of emission is greater than  $8^\circ$ . Both range and angle of emission are measured in the emulsion stack. This determines the kinematics. The protons of the  $\pi^0$  production process are limited to a forward angular cone. An isotropic component, believed to be due to gas impurities and equal to about 10 per cent of the  $\pi^0$  effect is subtracted. Absolute cross sections have not been given. The excitation function, shown in Figure 6, contains all events between  $53^\circ$  and  $143^\circ$  for the meson in the center of mass system. It is therefore very nearly the excitation function of the total cross section. Again the steep energy dependence near threshold is evident. The angular distribution, in agreement with the results of Cocconi & Silverman, is peaked at and symmetrical about  $90^\circ$  (Fig. 7).

The results have been extended to higher energies by Walker, Oakley & Tollestrup (72) using the techniques of Silverman & Stearns (69). As shown in Figure 6, the excitation function at  $90^\circ$  in the laboratory reaches a maximum of 18 microbarns per steradian for photons of 320 Mev and falls off sharply with increasing energy to one quarter of this value at 450 Mev. The corresponding high energy decrease of the total cross section is expected to be less severe because of a shift in the peak of the angular distribution towards the forward angles with increasing energy (73), and, to a lesser extent, because of changes with energy in the relationship of center of mass and laboratory systems.

*Charged photomeson production.*—The experimental study of charged photomesons was initiated by McMillan, Peterson & White (74). They detected mesons of both charges produced by x-rays from the Berkeley synchrotron in a carbon target, using nuclear emulsion detectors.  $\pi^+$  production in hydrogen was first investigated by Bishop, Cook, & Steinberger

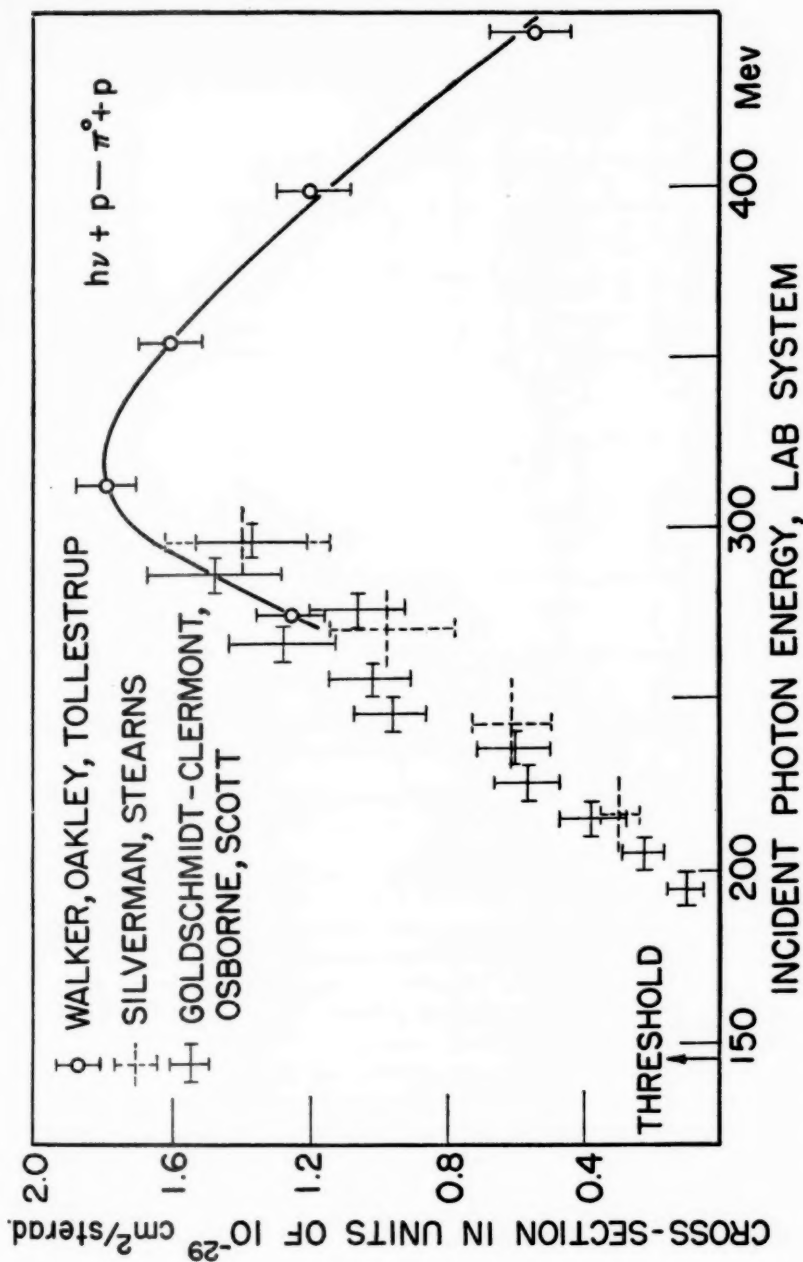


FIG. 6. Excitation function for photoproduction of  $\pi^0$  mesons in hydrogen. The data of Walker, Oakley & Tollestrup and of Silverman & Stearns was taken at  $90^\circ$  in the laboratory system. The data of Goldschmidt-Clermont, Osborn & Scott represent the total production between  $53^\circ$  and  $143^\circ$  in the center of mass system and are arbitrarily normalized.

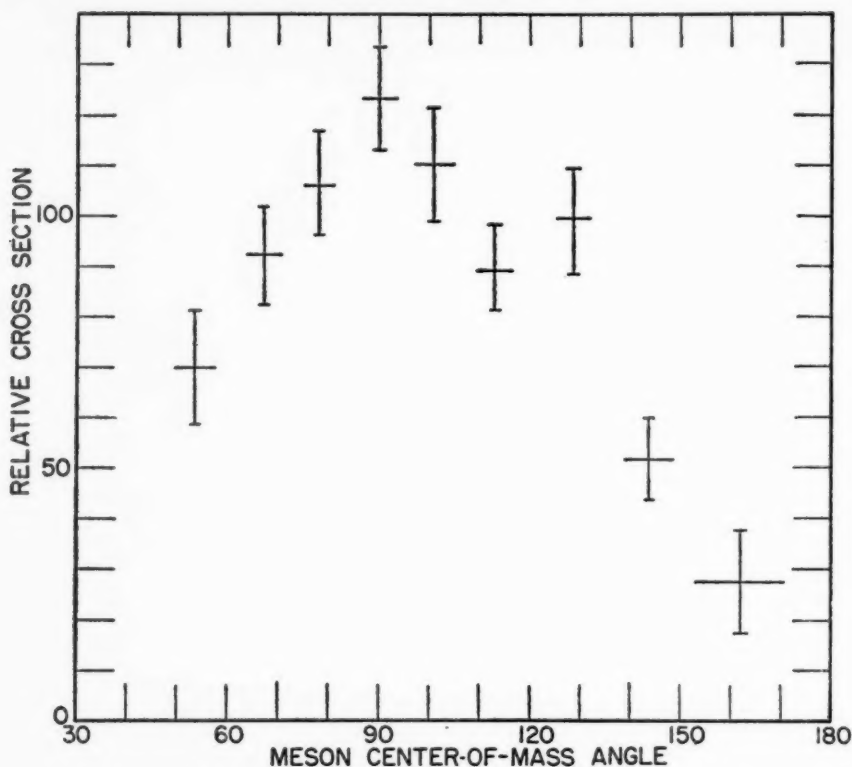


FIG. 7. Angular distribution in the center of mass system for  $\pi^0$  mesons produced in the reaction  $\gamma + P \rightarrow \pi^0 + P$ . The complete x-ray spectrum contributions up to a maximum energy of 320 Mev are included (71).

(75, 76, 77). In these experiments the 325 Mev max. energy x-ray beam was incident on a target of liquid hydrogen. The meson detector consisted of an aluminum absorber to slow the meson, and a crystal telescope.  $\pi^+$  mesons reaching the end of their range are identified by means of the positron which appears later, in the time characteristic of  $\mu$  decay. The errors are chiefly of two sorts: (a) Measurement of absolute cross sections requires a calibration of the efficiency with which the decay positrons are detected, in addition to the x-ray beam calibration. (b) The relative production at different meson energies requires a knowledge of the behavior of the mesons in various thicknesses of absorber. Mesons may disappear due to nuclear absorption and scattering in and out of the detector. The nuclear absorption may be estimated by using measured cross sections; however, the scattering is more difficult to evaluate. The results (Fig. 8 and Table IX) consist of an excitation function at  $90^\circ$  in the laboratory system and of the differential cross sections at several angles between  $58^\circ$  and  $158^\circ$ . The cross section at  $90^\circ$



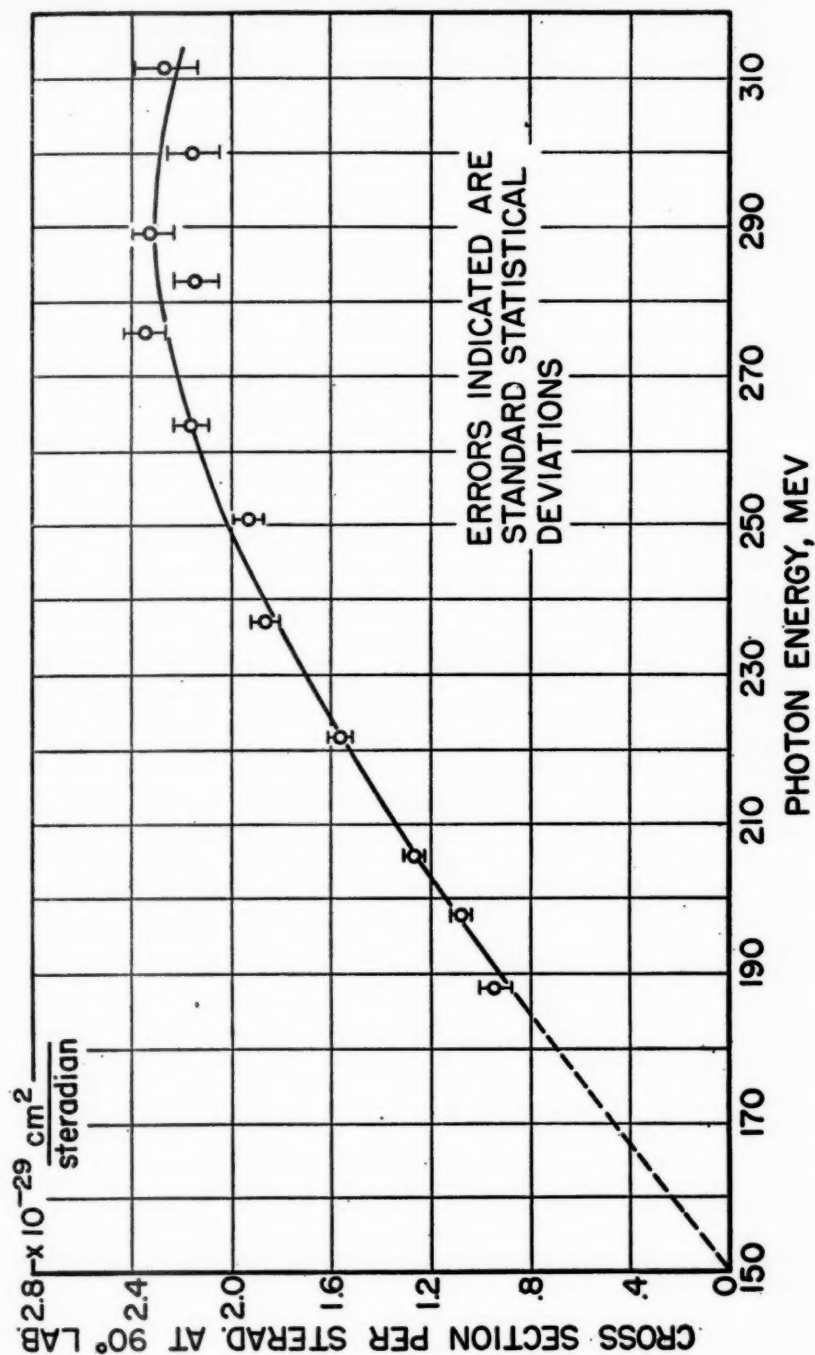


FIG. 8. Excitation function for the production of  $\pi^+$  mesons in hydrogen at  $90^\circ$  in the laboratory system. Steinberger & Bishop (77).

TABLE IX

PRODUCTION OF  $\pi^+$  MESONS IN HYDROGEN BY 255 MEV PHOTONS (77)

Center of Mass Angle, Degrees	58°	75°	93°	108°	122°	133°	145°	158°
$d\sigma/d\Omega$ (liquid H) $\mu\text{b/sterad.}$	14.7 $\pm 1.5$	17.4 $\pm 1.2$	17.4 $\pm 1.0$	20 $\pm 1.1$	17.4 $\pm 1.0$	20 $\pm 1.1$	17.4 $\pm 1.3$	13.5 $\pm 1.0$

Center of Mass Angle, Degrees	57°	82°	106°	127°	147°
$d\sigma/d\Omega$ ( $\text{CH}_2-\text{C}$ ) $\mu\text{b/sterad.}$	13.0 $\pm 1.2$	15.7 $\pm 1.7$	19.7 $\pm 1.3$	18.7 $\pm 1.3$	15.9 $\pm 1.1$

risers fairly linearly to a plateau of 22 microbarns per steradian between 260 and 310 Mev, the highest measured energy. For 255 Mev photons the production is chiefly into the back hemisphere with a broad maximum of 20 microbarns per steradian between 100° and 140°.

Goldschmidt-Clermont, Osborne & Winston (78) have reported the angular distribution at two photon energies, 270 Mev and 320 Mev. The technique is similar in physical arrangement to that of the Berkeley group. It differs in the use of carbon and paraffin targets and a short ( $10^{-6}$  sec.) beam pulse. The decay electrons are detected after the beam pulse, when the background radiation has in large measure disappeared. This permits observation at small production angles where background conditions were previously prohibitive. At high photon energies and small production angles, however, the meson range becomes comparable to the mean free path for nuclear absorption, so that errors already discussed may be serious. Results are given in Figure 9, and Table X. Absolute cross sections have not been reported.

TABLE X

PRODUCTION OF  $\pi^+$  MESONS IN HYDROGEN BY 320 MEV PHOTONS (78)

Center of Mass Angle, Degrees	30°	90°	150°
$d\sigma/d\Omega$ (relative)	.33 $\pm$ .12	1.00 $\pm$ .12	1.21 $\pm$ .12

Jenkins *et al.* (79) have measured the meson energy by magnetic deflection, and therefore avoid the difficulty of attenuation in the absorber. Their absolute calibration is probably the most reliable. Results are shown in Tables XI and XII.



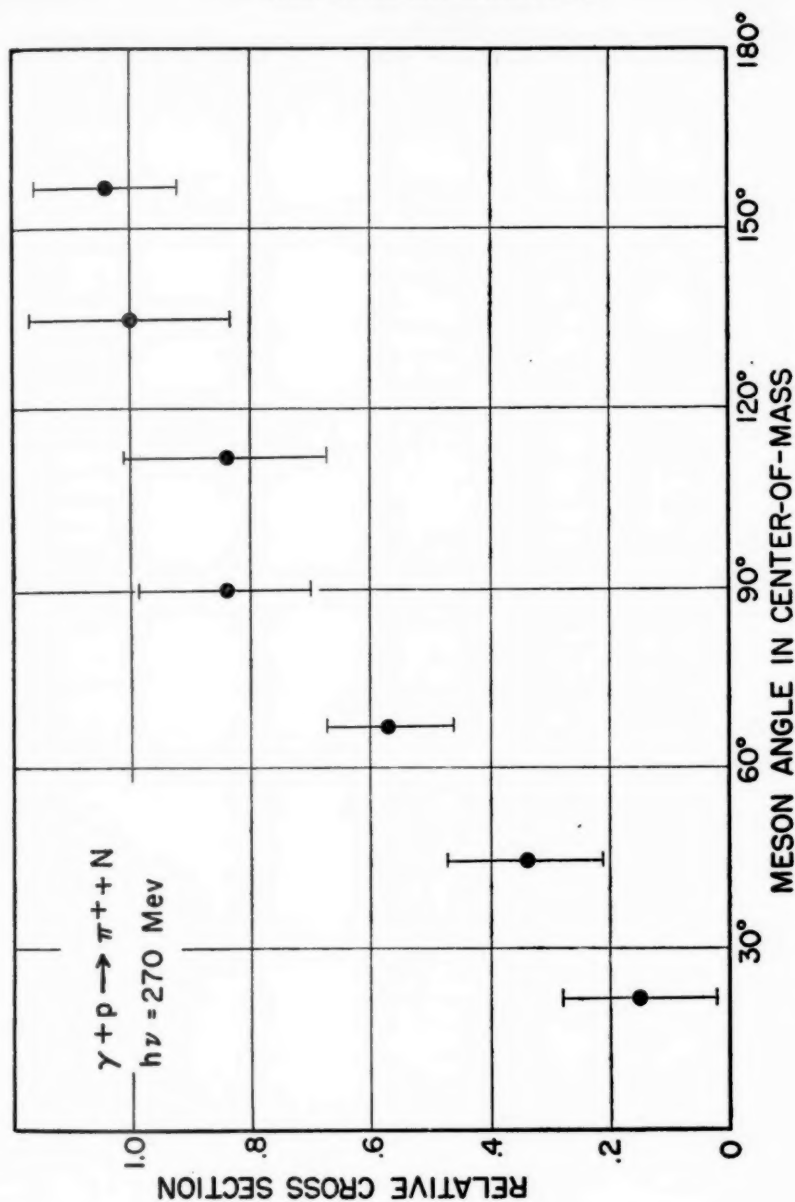


FIG. 9. Angular distribution in the center of mass system for the photoproduction of  $\pi^+$  mesons in hydrogen at 270 Mev (78).

TABLE XI  
PHOTOPRODUCTION FROM HYDROGEN OF  $\pi^+$  MESONS AT  
90° IN THE LABORATORY (79)

$E_\gamma$ , Mev	202	217	234	258	283
$d\sigma/d\Omega$ $\mu\text{b/sterad.}$	$14 \pm 2$	$16 \pm 2$	$18 \pm 1$	$23 \pm 1$	$22 \pm 1$

TABLE XII  
PRODUCTION OF  $\pi^+$  IN HYDROGEN BY 234 MEV PHOTONS (79)

Center of Mass Angle, Degrees	37°	106°	180°
$d\sigma/d\Omega$ $\mu\text{b/sterad.}$	$10 \pm 1$	$19 \pm 1$	$18 \pm 3$

TABLE XIII  
RATIO OF CROSS SECTIONS FOR THE PRODUCTION OF  $\pi^-$  AND  $\pi^+$   
MESONS FROM DEUTERIUM

Maximum x-ray Energy, Mev	325 (80)							
Laboratory Angle, Degrees	45	45	45	45	90	90	135	135
Meson Energy, Mev	43	57	87	128	34	70	39	57
$d\sigma(\pi^-)/d\sigma(\pi^+)$	.79 $\pm .21$	1.04 $\pm .16$	.89 $\pm .21$	.99 $\pm .10$	1.24 $\pm .201$	.98 $\pm .14$	1.37 $\pm .22$	1.05 $\pm .18$
Mean Value of Ratio	.96 $\pm$ .10				1.04 $\pm$ .12		1.21 $\pm$ .17	

Maximum x-ray Energy, Mev	330 (81)		315 (82)	320 (79)
Laboratory Angle, Degrees	26	90	135	30, 90, 180
Meson Energy, Mev			65 $\pm$ 15	All
$d\sigma(\pi^-)/d\sigma(\pi^+)$	.90 $\pm$ .23	.5 $\pm$ .5	1.19 $\pm$ .12	1.3 $\pm$ .2
Mean Value of Ratio				1.3 $\pm$ .2

*Photoproduction in deuterium (Photoproduction from neutrons).*—The study of the photoproduction of mesons from neutrons is not possible directly. However some information may be obtained from photoproduction in deuterium. The available information is collected in Tables XIII, XIV, XV.

TABLE XIV  
RATIO OF CROSS SECTIONS FOR THE PRODUCTION OF  $\pi^+$  MESONS  
FROM DEUTERIUM AND HYDROGEN

Maximum x-ray Energy, Mev	325 (80)					315 (81)	320 (79)
Laboratory Angle Degrees	26	45	90	90	135	135	30, 90, 180
Meson Energy Mev	65-145	38-134	40-105	39-93	37-67	65 $\pm$ 15	
$d\sigma(D)/d\sigma(H)$	.89 $\pm$ .17	.74 $\pm$ .08	.64 $\pm$ .18	.74 $\pm$ .05	.89 $\pm$ .06	.87 $\pm$ .07	.80 $\pm$ .10

TABLE XV  
RATIO OF CROSS SECTIONS FOR THE PRODUCTION OF  $\pi^0$  MESONS  
FROM DEUTERIUM AND HYDROGEN (70)

Maximum x-ray Energy, Mev	310					
Laboratory Angle, Degrees	45	70	90	120	135	150
$d\sigma(D)/d\sigma(H)$	1.76 $\pm$ .20	2.03 $\pm$ .17	1.01 $\pm$ .09	1.53 $\pm$ .17		

The ratio  $[d\sigma(\gamma + D \rightarrow \pi^+)/d\sigma(\gamma + H \rightarrow \pi^+)]$  is approximately .8 for all measured angles and energies. The near unity ratio indicates that positive photomeson production is only slightly altered by the presence of the neutron in the deuteron. This result is important for the interpretation of  $\pi^-$  and  $\pi^0$  photoproduction from deuterons. Since the  $\pi^+$  production from a free proton is similar to that of one bound in a deuteron,  $\pi^-$  production from free and deuterium-bound neutrons is expected to be similar. Table XIII lists the experimental results on the ratio of positive and negative mesons

produced in deuterium. The ratio is close to 1 at all measured angles and energies. This indicates that  $\pi^-$  production from free neutrons is closely equal to that of positive mesons from protons. Indeed, even if the presence of the additional nucleon had a marked effect on the photoproduction contrary to the experimental result for the ratio  $[d\sigma(\gamma + D \rightarrow \pi^+)]/[d\sigma(\gamma + H \rightarrow \pi^+)]$ , the effects of binding, exclusion, and multiple meson scattering enter symmetrically into  $\pi^-$  and  $\pi^+$  production from deuterium. Therefore even then, equal cross sections for the free nucleons would result in the observed unity ratio for  $\pi^-/\pi^+$  production from deuterium.

In the photoproduction of neutral mesons in deuterium, interference between proton- and neutron-produced mesons introduces a complication not present for charged mesons. The experimental ratios for  $[d\sigma(\gamma + D \rightarrow \pi^0)]/[d\sigma(\gamma + H \rightarrow \pi^0)]$  are given in Table XV. The ratio is close to two, and not incompatible with comparable production from free neutrons and protons.

*Angular momentum analysis.*—As in the analysis of meson scattering experiments, it is useful to assume that only a few angular momentum states contribute to the photoproduction of mesons. Then, parity and momentum conservation simplify the description of the production process, as shown by Brueckner & Watson (83) and by Feld<sup>6</sup> (84) (Table XVI).

<sup>6</sup> We shall show here how to obtain the angular distribution for the case of magnetic dipole absorption in a state of total angular momentum  $J=3/2$ , and emission of the meson in a  $p$  state. The derivation is simpler for the inverse process of  $\pi + N \rightarrow \gamma + N$ , where  $N$  is either nucleon. (By detailed balancing the angular distributions for the direct and inverse processes are alike.)

If the direction of the incident meson is chosen as the  $z$ -axis, its angular momentum about this axis is zero. The component of the total angular momentum along the  $z$ -axis is thus  $+\frac{1}{2}$ , if the initial nucleon spin direction is along the positive  $z$ -axis. The  $z$ -component of the final proton spin is either  $+\frac{1}{2}$  or  $-\frac{1}{2}$ . The  $z$ -component of the  $\gamma$ -ray angular momentum is therefore 0 or  $+1$ , respectively. The amplitude of the process is then given (83a, p. 792) by

$$A\alpha\sqrt{2/3} X_{10} + \sqrt{1/3} X_{11},$$

where  $X_{lm}$  are vector spherical harmonics defined (83a, p. 798) by

$$X_{lm} = -irx\nabla \frac{Y_{lm}(\theta, \phi)}{\sqrt{l(l+1)}}.$$

Here  $Y_{lm}$  are the normal scalar spherical harmonics. Use of the orthogonality properties of the vector spherical harmonics together with the relation (83a, p. 594)

$$\begin{aligned} X_{lm}^* \cdot X_{lm} = & 1/2 \left[ 1 - \frac{m(m+1)}{l(l+1)} |Y_{l,m+1}|^2 \right] + 1/2 \left[ 1 - \frac{m(m-1)}{l(l+1)} |Y_{l,m-1}|^2 \right] \\ & + \frac{m^2}{l(l+1)} |Y_{l,m}|^2 \end{aligned}$$

leads to a cross section with an angular distribution given by  $2+3 \sin^2 \theta$ . The results for other entries in Table XVI may be derived similarly.

TABLE XVI

ANGULAR AND ENERGY DISTRIBUTIONS IN THE PHOTOPRODUCTION  
OF  $\pi$ -MESONS ON NUCLEONS (84)

$\gamma$ -ray Absorbed	Intermed. State		$l$ of $\pi$ -Meson	$d\sigma/d\Omega(\theta)$	$\pi$ Momen- tum Depend- ence at Threshold
	$J$	Parity			
Magnetic dipole	1/2	+	1	constant	$k^3$
Magnetic dipole	3/2	+	1	$2+3 \sin^2 \theta$	$k^3$
Electric dipole	1/2	-	0	constant	$k$
Electric dipole	3/2	-	2	$2+3 \sin^2 \theta$	$k^5$
Electric Quadrupole	3/2	+	1	$1+\cos^2 \theta$	$k^3$
Electric Quadrupole	5/2	+	3	$1+6 \cos^2 \theta$ $-5 \cos^4 \theta$	$k^7$

The angular distribution of emitted mesons is determined by both the multipole character of the absorbed radiation and the total angular momentum. On the other hand, the energy variation of the cross section near threshold depends only on the orbital angular momentum of the emitted meson.

The dependence of the cross section near threshold on the meson momentum is linear for production into  $s$  states and cubic into  $p$  states. The observed excitation function for  $\pi^0$  mesons shows that there can be little  $s$  state production and is compatible with pure  $p$  state. The symmetry of the angular distribution about  $90^\circ$  makes it even more likely that in good approximation only  $p$  state neutral mesons are produced near threshold. This leaves three possibilities: magnetic dipole absorption with  $J=1/2$  and  $J=3/2$ , and electric quadrupole absorption with  $J=3/2$ . If only one of these contributes, the observed peaking of the angular distribution about  $90^\circ$  requires that it be magnetic dipole with  $J=3/2$ . The possible importance of this state has been previously discussed in the section on Meson-nucleon scattering. However, as in the scattering, the data can also be fitted with magnetic dipole absorption into a  $J=1/2$  state if some  $J=3/2$  state is also present. In general, for magnetic dipole absorption, the angular distribution is given by

$$\frac{d\sigma}{d\Omega} = |a_{3/2}|^2(1 + 3/2 \sin^2 \theta) + |a_{1/2}|^2 - 2 \operatorname{Re} a_{1/2} a_{3/2}^*(1 - 3/2 \sin^2 \theta).$$

Here  $a_J$  is the amplitude for the production process into a given total angular

momentum state,  $J$ . This equation has a double valued solution, which for the experimental  $\pi^0$  emission cross section corresponds to either

$$a_{3/2} \gg a_{1/2} \quad \text{or} \quad a_{1/2} \gg a_{3/2}.$$

In the case of  $\pi^+$  production the excitation function requires some  $s$  state, and the asymmetry of the angular distribution about  $90^\circ$  necessitates even-odd wave interference. The production near threshold is therefore chiefly into  $s$  and  $p$  states. Only electric dipole absorption contributes to  $s$  state production. The relative contribution of  $s$  and  $p$  states cannot be ascertained without additional assumptions.

In summary, the outstanding features of the photomeson production from hydrogen are:

- (a) Near threshold, the  $\pi^0$  production is chiefly in  $p$  states.
- (b) The  $\pi^0$  angular distribution is consistent with pure magnetic dipole absorption into a mixture of  $J = 1/2$  and  $J = 3/2$  states, with either  $J = 3/2$  or  $J = 1/2$  state prominent.
- (c) The experiments suggest, but with large uncertainty, comparable production of  $\pi^0$  mesons from neutrons and protons.
- (d) For 255 Mev photons the total  $\pi^0$  cross section is approximately one fourth that for  $\pi^+$ .
- (e) The production of positive mesons is preferentially into the backward hemisphere, so that both even and odd states must contribute.
- (f) The  $\pi^+$  production from protons and  $\pi^-$  production from neutrons are approximately equal.

*Isotopic spin analysis.*—An analysis based on isotopic spin conservation in the meson-nucleon interaction was suggested by Watson (39) even though isotopic spin is not expected to be a good quantum number in photomeson production. When the electromagnetic field is neglected, the Hamiltonian is a scalar under rotations in charge space. If the interaction of the photon with the nucleon current and moment and the meson current is treated as a small perturbation, it transforms in charge space like a linear combination of a scalar,  $S$ , and the  $z$  component of a vector,  $V_z$ . The initial nucleon has  $T = 1/2$ , so that the scalar interaction connects this state only to a final state of  $T = 1/2$ .  $V_z$ , on the other hand, connects the initial  $T = 1/2$  state to final states with both  $T = 3/2$  and  $1/2$ . In fact, if the  $z$ -component of  $T$  is referred to as  $m$ , then (86)

$$\begin{aligned} (1/2, m' | V_z | 1/2, m) &= \delta_{mm'} m V^{1/2} \\ (3/2, m' | V_z | 1/2, m) &= \delta_{mm'} \sqrt{2} V^{3/2} \\ (1/2, m' | S | 1/2, m) &= \delta_{mm'} S^{1/2}. \end{aligned}$$

Only the matrix  $(1/2, m' | V_z | 1/2, m)$  depends on whether the initial nucleon is a proton or neutron; in particular, transitions to a  $T = 3/2$  state are independent of the initial nucleon charge state.

If it is assumed that only electric and magnetic dipole radiations are absorbed, then 12 independent matrix elements are necessary to describe

the production of mesons by photons. Charge independence implies three relations among these, leaving nine independent matrix elements. Present experimental results are hopelessly inadequate to determine these.

Brueckner & Watson (83) have made several additional arbitrary assumptions to further reduce the number of matrix elements. They argue that the scattering data suggests that only  $T=3/2$  and therefore only  $V^{3/2}$  is important for mesons emitted into  $p$  states. This assumption is sufficient to predict meson production into  $p$  states with ratios:

$$1 = \frac{\gamma + p \rightarrow \pi^0 + p}{\gamma + n \rightarrow \pi^0 + n} = \frac{\gamma + p \rightarrow \pi^+ + n}{\gamma + n \rightarrow \pi^- + p} = 2 \frac{\gamma + p \rightarrow \pi^+ + n}{\gamma + p \rightarrow \pi^0 + p}.$$

This is not in disagreement with experiments. Further, experiments show that  $\pi^0$  mesons are produced almost entirely in  $p$  states. This requires that, in the  $s$  state,  $2 V^{3/2} = 1/2 V^{1/2} - S^{1/2}$ . In addition, it is assumed that of the remaining matrix elements in the  $p$  state, that with  $J=1/2$  is zero. For photoproduction from protons this leaves only two independent matrix elements. The angular distributions are (83):

$$\begin{aligned} \frac{d\sigma}{d\Omega}(\gamma + p \rightarrow \pi^0 + p) &\propto (2 + 3 \sin^2 \theta) |b|^2 \\ \frac{d\sigma}{d\Omega}(\gamma + p \rightarrow \pi^+ + p) &\propto (2 + 3 \sin^2 \theta) |b|^2 + 9 |a|^2 + 6\sqrt{2} \cos \theta \operatorname{Im} a^* b, \end{aligned}$$

where  $b = \sqrt{2} V^{3/2}$  for  $p$  states with  $J=3/2$  and all other  $p$  state matrix elements are zero, and  $a = 2 V^{3/2} = 1/2 V^{1/2} - S^{1/2}$  for  $s$  states. The angular distribution for  $\pi^0$  mesons is now  $2 + 3 \sin^2 \theta$ , in satisfactory agreement with experiment (Fig. 6). Proper choice of the remaining matrix element for production into  $s$  states,  $a$ , allows a fit of the  $\pi^+$  data as well (66, 78).

*Theory.*—In the photoproduction of mesons the incident quantum can interact either with the currents of the heavy proton or lighter charged mesons. The latter are expected to give the main contribution to the photon interactions as long as the nucleon velocities are non-relativistic. Since the neutral meson has no electromagnetic interaction, it is striking that the  $\pi^0$  photoproduction is comparable to that for  $\pi^+$  and  $\pi^-$ , except very near threshold. This large neutral meson cross section implies a strong coupling between the charged and neutral meson fields around a nucleon.

If recoil and nucleon pairs are neglected, pseudoscalar mesons can be emitted into (or absorbed from)  $p$  states only. A large interaction between charged and neutral mesons in  $p$  states arises from their mutual coupling to the nucleon Pauli and isotopic spins. An electric dipole photon, when absorbed by a charged  $p$  state meson, induces transitions into  $s$  or  $d$  states. If mesons in both of these states are assumed to have negligible interaction with the nucleon, neutral mesons will not be produced by electric dipole photons. On the other hand, the absorption of magnetic dipole radiation does not change the magnitude of the meson orbital angular momentum. The  $p$  state charged meson can therefore be scattered by the nucleon before



it is emitted as a free meson. A neutral meson may be produced when the meson-nucleon scattering gives charge exchange.

This feature was first evident in a strong coupling calculation of Fujimoto & Miyazawa (87) and later in similar calculations by Brueckner & Case (88) and others. These calculations give a resonance for the  $p$  state meson-nucleon interaction in  $J=3/2$ ,  $T=3/2$ . For an appropriate adjustment of source size and coupling strength this resonance occurs at about 200 Mev compatible with meson-nucleon scattering data. If the meson-nucleon system interacts weakly in other states, magnetic dipole and electric quadrupole absorption will be mostly into  $J=T=3/2$ . It has already been pointed out that in this state neutral mesons are twice as probable as charged. It is a feature of these calculations, therefore, that in  $p$  states approximately twice as many neutral as charged mesons are produced. Predominance of magnetic dipole absorption peaks the angular distribution at  $90^\circ$  in satisfactory agreement with experiment. The resonance would also give the maximum in the neutral photomeson excitation function near 350 Mev which is suggested by the California Institute of Technology data (Fig. 6). However, it must be remembered that, in the meson scattering theory of Chew, a main feature of the strong coupling scattering is preserved, viz., a dominant  $T=J=3/2$  interaction. Nevertheless, depending on the detailed choice of constants, the corresponding meson scattering phase shift may or may not reach  $90^\circ$ . Likewise, in the photoproduction, an intermediate coupling treatment may retain the main qualitative features but dispense with the resonance of the strong coupling calculation.

The radius of the  $p$  wave meson cloud is  $\hbar/\mu c$ , which is greater than  $\lambda/2\pi$  for the incident quanta. Therefore, higher multipole radiation may contribute significantly to charged meson photoproduction. However, the charge exchange scattering is assumed to take place only in  $p$  states, so that magnetic dipole and electric quadrupole absorption alone are relevant for  $\pi^0$  production.

For charged mesons the gradient coupling theory gives approximately the same angular distribution in weak, intermediate (89), and strong coupling calculations (87). The differential cross section is predominantly flat because of large  $s$  wave production from electric dipole absorption. Other multipole photons and  $d$  wave mesons from electric dipole radiation give a small dip at  $\cos \theta = (1 - \sqrt{1 - \beta^2}) \beta^{-1}$  in the center of mass system. Here  $\beta$  is the meson velocity divided by  $c$ . This distribution is considerably flatter than that obtained experimentally.

As long as nucleon recoil is neglected, all calculations based on a charge symmetric meson theory give a  $\pi^+/\pi^-$  ratio of one, and equal  $\pi^0$  production from protons and neutrons. The absorption of the photon is through the charged meson cloud which, in the symmetric theory, differs only in the sign of its charge for proton and neutron. Recoil has been properly taken into account only in the perturbation theory. The current of the recoil proton interacts mainly with electric dipole photons. For high meson energies



it contributes a large  $\pi^-/\pi^+$  ratio in the backward direction (90). The approximate unit value of the experimental ratio implies that high order corrections will reduce the importance of nucleon recoil currents. The fact that the anomalous nucleon magnetic moments are approximately equal but of opposite sign for neutrons and protons would also follow only if the nucleon currents introduce no substantial asymmetry in the electromagnetic interaction.

In the pseudoscalar coupling theory an important role is played by antinucleons so that a strong coupling approach has not proved possible. Only perturbation theory calculations have been performed. In this limit the results are identical with those of the gradient coupling theory and in violent disagreement with the experiments on  $\pi^0$  production. However closer agreement with experiment may come from the terms neglected in the perturbation theory. In the meson scattering calculations, by including some of these terms in pseudoscalar coupling theory, the Cornell group was able to obtain  $p$  wave scattering qualitatively similar to that of Chew and to the strong coupling calculations in gradient coupling theory. It is entirely possible that similar agreement will be obtained for photoproduction into  $p$  states, but the calculation has not been performed.

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## MESONS AND HEAVY UNSTABLE PARTICLES IN COSMIC RAYS<sup>1</sup>

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The first part of this paper is a summary of the main experimental data about heavy mesons and other particles observed in cosmic rays. The second part, written immediately after the International Meeting on Cosmic Radiation held in Bagnères-de-Bigorre, France in July, 1953, gives the latest experimental data and a few attempts at interpretation of the results as a whole.

The first published observation on the possible existence of a particle of mass between those of the  $\pi$ -meson and proton in cosmic rays was given in 1944 by Leprince-Ringuet & Lhéritier (1): in a cloud chamber picture, a positive particle collides with an electron and gives it a large energy; assuming the collision to be elastic, one gets for the positive particle a mass  $990 \pm 100 m_e$ ,  $m_e$  being the electron mass.

One should notice that the identification of this particle was made by a collision and not by an intrinsic characteristic (decay in flight or at rest, for example). It is therefore impossible to know which kind of heavy meson it was; one can only tell that its mean life was at least of the order of  $10^{-9}$  sec. by looking at the length of the trajectory.

The following information was obtained by Rochester & Butler from a cloud-chamber study (2): two outstanding pictures give the first indication for heavy particles disintegrating in flight, i.e.,  $V$ -events. One of them is a case of a charged particle decaying into another particle of the same charge, together with one or more neutral particles; the other is a case of a neutral particle coming from a high-energy nuclear interaction and decaying in the cloud-chamber gas into two particles of opposite signs in a  $V$ -like shape: it is the first example of a neutral  $V$ -event.

The third piece of information was obtained by the Bristol group while studying cosmic radiation with minimum ionization sensitive photographic emulsions (3). The analysis of this event is given at the beginning of the  $\tau$ -meson chapter. It is remarkable enough to convince one of the very probable existence of a heavy meson of mass about 1,000 which disintegrates into three mesons.

In 1951, Rossi and co-workers obtained pictures of an event type which they called  $S$ , by means of a multiple-screen cloud chamber (4). A typical picture shows a heavy meson stopping in a screen and producing a secondary visible particle which is also a meson.

Later in 1951 O'Ceallaigh obtained the first pictures with photographic

<sup>1</sup> The survey of the literature pertaining to this review was concluded in July 1953, but is not exhaustive.

plates of  $\kappa$ -type mesons; they disintegrate in the emulsion into an ionizing secondary.

We are going to deal successively with these several types of particles, giving mainly the results obtained in 1952 and the beginning of 1953.

### $\tau$ -MESONS

The tau-meson ( $\tau$ -meson) was the first heavy meson the identification of which was made certain in photographic emulsions. The first observation, by the Bristol group in 1949, is very remarkable as all by itself it provides a convincing evidence of the existence of a new well-defined particle (3). It gives the following information: a track more than  $2,000 \mu$  long ends in P (Fig. 1).

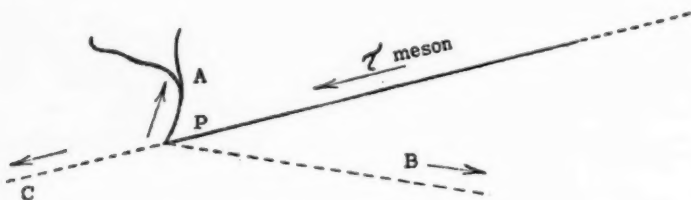


FIG. 1. First observation of a  $\tau$ -meson.

Its direction of travel is well defined because of its length, and a direct mass measurement on it gives something around  $1000 m_e$ . Three tracks issue from point P: one of them, PA, is that of a  $\pi$ -meson because of the two heavy-prong star produced at its end A. The track PB is that of a  $\pi$ - or  $\mu$ -meson, but PC is too short to be well identified. Furthermore, the three tracks coming from point P are coplanar within less than 4 degrees. The chance coincidence between the end of a heavy meson track and the center of a three coplanar prong star is practically impossible. One could hesitate between two explanations: the disintegration of a nucleus absorbing a heavy meson, and the spontaneous decay of a heavy meson. The fact that there are at least two, or maybe three, mesons coming from P, the coplanarity of the three tracks, and the momentum balance assuming three  $\pi$ -mesons, are very much in favor of a spontaneous decay.

More than a year later, two similar events were found in London in 1950, and two others in 1951 in Bristol (6, 7, 8). In 1952, a particularly well defined event, the  $\tau_{P_1}$ -meson, was observed in Padua coming from a star, and since then three other  $\tau$ -mesons were observed in Bristol, Milan, and Padua; the last one coming also from a star (9, 10, 17). As one can see, the number of these events is very small even though the detection is particularly easy because of the coplanarity of the tracks. In spite of that, the  $\tau$ -meson is, among the heavy mesons, the one whose mass is by far the most precisely measured and for which the  $Q$ -value of the disintegration is best known.

Table I sums up the main results, which we now discuss.

TABLE I  
DATA ON  $\tau$  MESONS OBSERVED IN EMULSIONS\*

	Primary		Secondaries		Total Kinetic Energy (Mev) Assuming $3\pi$	Observation Altitude
	Length in Microns	Mass in $m_e$	Length of the Tracks	Masses		
$\tau_{B_1}$	3,100	$\sim 1,000$	45 2,100 116	$\pi$ ( $\sigma$ star)  $280 \pm 30$	$65 \pm 6$	3,450 m.  10 cm. lead
$\tau_{B_2}$	2,070	$\sim 1,000$	6,400 120 490	$285 \pm 20$	$75 \pm 4$	3,450 m.  30 cm. lead
$\tau_{L_1}$	740	$> \pi$	1,300 420 30	$\pi$ or $\mu$	$76 \pm 15$	3,450 m.  0.9 m. of ice
$\tau_{L_2}$	1,900		short tracks			3,450 m. 0.9 m. of ice
$\tau_{L_3}$			990 720 445		$73.5 \pm 7$	3,450 m.  3 m. of ice
$\tau_{P_1}$ coming out from a star	8,000	$970 \pm 100$	2,600 2,000 150		$86.5 \pm 5$	27,000 m.  5 cm. Al.
$\tau_{B_3}$	420		short tracks			27,000 m.
$\tau_M$	4,000	$890 \pm 180$	162 2,500 640	$\pi \rightarrow \mu \rightarrow e$  $270 \pm 43$	$75 \pm 7$	25,000 m.
$\tau_{P_2}$ coming out from a star	$5,300 \pm 2,000$	$955 \pm 110$	4,100 1,800 $520 + 2,350$		$78 \pm 5$	30,000 m.

\* B, L, M, P=Bristol, London, Milan, Padua.

*Direct mass measurement for  $\tau$ -mesons.*—The longest primary tracks are those of the  $\tau_{P_1}$ ,  $\tau_M$  and  $\tau_{P_2}$ , respectively 8,000, 4,000 and 7,300  $\mu$  long. They afford a mass determination by scattering-range and ionization-range measurement. One gets respectively  $970 \pm 100$ ,  $890 \pm 180$ , and  $955 \pm 110$ . In the other cases, one can just say that they are of the order of 1,000.

*Identification of secondary particles.*—One should keep in mind the following information: (a) In two cases, one of the secondary particles was found to be a  $\pi$ -meson from its decay ( $\sigma$ -star or  $\pi$ - $\mu$ - $e$ ). (b) In a few cases, the mass of a secondary particle could be measured from scattering-ionization in favorable conditions. The results are  $280 \pm 30$ ,  $285 \pm 20$ , and  $270 \pm 43$ . For the two long secondary tracks coming from the  $\tau_{P_1}$ , direct measurements have not been published. One sees that the above values are in favor of a  $\pi$ -



rather than a  $\mu$ -meson. (c) By measuring the ionization (then the velocity) of each secondary particle of an event and combining them with track angle measurements, one can get the mass ratio of the secondary particles. That was done for nearly all the  $\tau$ -mesons and always gave mass ratios around one. For instance, for the  $\tau_{L1}$ , one gets the following relative mass values for the secondary particles:  $1.05 \pm 0.2$ , 1, and  $0.96 \pm 0.25$ . (d) More information could be obtained from the  $\tau_{P1}$  owing to the great length of two of the three tracks. For that, one assumes that the secondary particles can be either  $\pi$ -, or  $\mu$ -mesons and one computes, for each of the possible combinations, the energy value of the tracks from the momentum conservation relation: the experimental values for the longest secondary track, assumed to be exact, are the starting point for these calculations. Then, the calculated values for tracks 2 and 3 are compared to experimental values and a few combinations can be excluded. The best schemes are  $3\pi$  or  $3\mu$ , but  $\pi\pi\mu$  is not excluded. A slightly different study on the  $\tau_{P2}$  gives similar results. (e) Finally, there is always coplanarity of the tracks (except in a very poor case), within less than two degrees in the best cases. There appear to be no neutral particles whatever, except perhaps a photon or a neutrino under 6 Mev. It is very improbable that such a particle, if emitted, ever takes more than 6 Mev.

To sum up: This body of information makes it nearly certain that the  $\tau$ -meson decays into three  $\pi$ 's without neutral particles, but the decay into  $2\pi + \mu$  is not absolutely excluded.

*Q-value of the  $\tau$ -meson decay.*—For each event, one can get the following information: angles between tracks, ionization of each track (and from this the velocity of each particle), and in a few cases only, a possible measurement of  $p\beta c$  by scattering. Furthermore, the total momentum of the three secondary particles must be zero. Then for an assumed mass for each particle, it is possible to calculate the  $Q$ -value of the decay. Assuming three  $\pi$ -mesons, one gets  $Q$ -values in agreement with each other.

One can write  $Q = (75 \pm 3.5)$  Mev. The  $\tau$ -meson mass follows immediately:  $M_\tau = (978 \pm 7)m_e$ , if one assumes the  $\pi$ -mass to be 277 (15). From recent evidence, it looks like the  $\pi$ -mass is lower by a few units; that would lower the  $\tau$ -mass by about ten units. Let us recall that these determinations are made assuming the  $\tau$ -meson decays into three  $\pi$ 's.

*Cloud chamber  $\tau$ -meson observations.*—A few events, interpreted as  $\tau$ -meson decays in flight, have been observed in the cloud chamber when studying penetrating showers (11, 12, 13, 14). In one of them (11) the three secondary momenta are  $155 \pm 30$ ,  $350 \pm 75$ , and  $210 \pm 50$  Mev/c. Assuming three  $\pi$ -mesons, the kinetic energy is around 75 Mev and the  $\tau$ -mass is around  $975 m_e$ , which is in good agreement with the photographic emulsion observations. The other event observed by the same group, as well as by two other groups, does not yield such good measurements because of the high energies of the secondary tracks.

*$\tau$ -meson mean lifetime.*—Little valuable information is available from



photographic emulsion work on the  $\tau$ -meson mean lifetime. One can make an estimation from the proportions of  $\pi$ - and heavy mesons stopping in the emulsion (8). In this way, one estimates  $\tau_0 \geq 10^{-9}$  sec. Other experiments performed at the Jungfraujoch under various ice thicknesses yield comparable results (16). Finally, cloud chamber experiments give good arguments for a value at least equal to  $10^{-9}$  sec. (11).

#### K-TYPE MESONS (EXCLUDING $\tau$ -MESONS)

*$\kappa$ -mesons.*—The first two  $\kappa$ -mesons ending in emulsions were discovered by O'Ceallaigh (5) in Bristol in 1951. While using emulsions to study the spectrum of the electrons coming from  $\mu$ -meson decay at rest, he found two unusual events:  $\kappa_{B1}$  and  $\kappa_{B2}$ . In the  $\kappa_{B1}$  case, the secondary particle energy, assumed to be an electron, is of the order of four times the spectrum maximum energy (i.e.,  $4 \times 55$  Mev.).

The mass measurement of the primary track,  $4,000 \mu$  long, gave a mass very much larger than the  $\mu$ 's:  $(1320 \pm 170 m_e)$ . So, it could not be a  $\mu$ - $e$  decay, in spite of its similar appearance. This event is the decay at rest of a heavy meson yielding a charged particle (electron,  $\mu$ - or  $\pi$ -meson) whose  $p\beta c$  is of the order of 250 Mev, with one or more neutral invisible particles.

In the  $\kappa_{B2}$  case, the secondary particle is a  $\mu$ -meson  $1,100 \mu$  long stopping in the emulsion and giving a decay electron. The length is well above that of a  $\mu$ -meson coming from a  $\pi$  at rest, i.e.,  $600 \mu$ . On the other hand, the primary, traced on the facing emulsion, has a mass  $1,125 \pm 150 m_e$ .

O'Ceallaigh concludes: (a) that there exist one or more mesons differing from the  $\tau$ -meson, with masses in the neighbourhood of  $1,000 m_e$ ; one of the secondary particles is a  $\mu$  of about 6 Mev, the other a charged particle of mass smaller than 400 and  $p\beta c$  around 250 Mev; (b) that in two other events belonging to the same type of decay, the decay yields one  $\mu$ -meson and at least two neutral particles.

The third  $\kappa$ -meson is  $\kappa_{P1}$  [Ecole Polytechnique, Paris (18)]. Its remarkable feature is the great length of the secondary ( $20,000 \mu$ ), which enables a precise momentum measurement,  $p\beta c = 197 \pm 13$  Mev, as well as a precise ionization measurement. It is very probably a  $\mu$ -meson. At the Bristol meeting, December 1951, four new  $\kappa$ -mesons were exhibited by the Bristol group and, shortly after, the number of mesons of this type stopping in the emulsion kept increasing [Bristol and Milan (19)].

*$\kappa$ - and  $\chi$ -mesons.*—At the Copenhagen meeting (June 1952), the main information given by Powell (20) was that in three or four cases out of a dozen, ionization and scattering measurements identify the secondary as being very probably a  $\pi$ -meson with a unique energy value  $110 \pm 10$  Mev, thus suggesting a decay into two particles only of a new heavy meson differing from the above ones. On the other hand, it looks like the new heavy meson mass is larger than that of the former one; these two particles, called respectively Chi ( $\chi$ ) and Kappa ( $\kappa$ ) would have the following characteristics:

Primary Particle	Mass in $m_e$	Mode of Decay
Kappa	$1,080 \pm 100$	$\mu$ + at least 2 neutral particles
Chi	$1,470 \pm 100$	$\pi$ + 1 neutral (mass $890 \pm 100$ )

In relation with this table, we add: (a) For the  $\kappa$  the continuous nature of the spectrum is well established, as two  $\mu$ 's have been identified with 6 and 34 Mev energies, one from its decay electron, the other from precise measurements in a case where the secondary is slow enough to be well differentiated from a  $\pi$ . Besides, other  $\mu$ 's can be quite well identified until  $p\beta c$  becomes of the order of 200 to 250 Mev. The primary  $\kappa$  mass is quite well measured directly in a few cases; (b) For the  $\chi$ , the best evidence is the identification of three secondary particles as being  $\pi$ 's with the same energy. But the basis of this identification is always ionization-scattering measurements; in no case is the  $\pi$  identified by a nuclear interaction or a  $\pi$ - $\mu$  decay.

Further, no primary  $\chi$  is long enough to yield a precise direct measurement of the mass.

By April 1953, about 30  $\kappa$ 's stopping in the emulsion had been identified. Six of these come from stars (two in Milan,  $M_2$  and  $M_3$ , one in Oslo,  $O_1$ , three in Paris  $P_2$ ,  $P_3$ ,  $P_4$ ). Table II gives the data for the main ones. Before giving interpretations, here are a few remarks about measurements.

(a) For the primary, one gets the mass value from scattering-range and ionization-range measurements; since the range is known, one gets two independent values. However, the scattering measurements are rather doubtful at the end of the range because of the fast decrease of the velocity and the difficulty of getting a precise and correct experimental method (practically, the last two 2,000  $\mu$  are hardly suitable for satisfactory scattering measurements).

Ionization measurements are precise enough in G5 Ilford emulsions only when far enough from the end of the range: they can be improved by using photometric methods (21, 22, 23, 24), provided they are well corrected and calibrated. The best range for mass measurement by ionization-range, for a particle of mass in-between proton and  $\pi$ -meson, is 2,500 to 6,000  $\mu$  from the end of the range.

These remarks show why only primaries longer than 2,000 to 3,000  $\mu$  should be taken into account for good mass determinations.

(b) For the secondary, the situation is different.  $p\beta c$  values are large, usually larger than 100 Mev. Ionization measurements are then precise (3 per cent in a few cases) when the length reaches several thousands of microns, but scattering measurements require great length because the optimum cell length is of the order of 100  $\mu$  and many cells are necessary. For this last reason the accuracy is small when the track is less than 3,000  $\mu$  long. So, for different reasons, the primary and the secondary will yield good data, us-

TABLE II  
MAIN TYPE  $\kappa$ -MESONS STOPPING IN THE EMULSION\*

No.	Primary			Secondary			
	Length in Microns	Mass by Scattering	Mass by Ionization	Length in Microns	Ionization Relative to Minimum	$p\beta c$ (Mev)	Type Mass
B <sub>1</sub>	4,100	1,260 ± 260		2,200	0.97 ± 0.04	250 ± 35	<400 certain
B <sub>2</sub>	5,670	1,125 ± 230		1,100		11.8	
B <sub>3</sub>	535			5,900	0.96 ± 0.026	157 ± 14	175 ± 25
B <sub>4</sub>	2,100	1,370 ± 320		170			
B <sub>5</sub>	1,540	1,000 ± 300		8,900	1.705 ± 0.083	66 ± 11	220 ± 15
B <sub>6</sub>	2,550	1,000 ± 240		150			
B <sub>7</sub>	380			2,500	1.090 ± 0.05	174 ± 29	270 ± 40
B <sub>8</sub>	2,550	1,460 ± 320		7,650	1.140 ± 0.025	192 ± 18	330 ± 30
B <sub>9</sub>	630			19,500	1.048 ± 0.025	168 ± 10	270 ± 18
B <sub>12</sub>	13,300	870 ± 100					
B <sub>14</sub>	3,300	800 ± 200					
B <sub>15</sub>	9,560	1,130 ± 170		4,100	1.028 ± 0.03	150 ± 20	
B <sub>16</sub>	1,700			2,640	0.95 ± 0.04	152 ± 24	
B <sub>17</sub>	4,230	1,200 ± 230		6,500	0.14 ± 0.018	175 ± 15	
P <sub>1</sub>	1,300			20,000	0.97 ± 0.03	197 ± 13	$\mu$ very probable
P <sub>2</sub>	4,950	850 ± 150	902 ± 80	155			
P <sub>3</sub>	6,040	1,065 ± 160	1,015 ± 85	some grains			
P <sub>4</sub>	9,000	920 ± 130	910 ± 75	850		> 50	
P <sub>5</sub>	1,600		800 ± 200				
P <sub>6</sub>	1,400	844 ± 230	958 ± 225	3,400	0.975 ± 0.05	290 ± 60	
M <sub>1</sub>	2,080	1,200 ± 240		840			
M <sub>2</sub>	5,260	1,040 ± 120		450			
M <sub>3</sub>	1,885	1,380 ± 210		840			
O <sub>1</sub>	14,000	950 ± 140		2,500	1.05 ± 0.03	126 ± 21	
K <sub>1</sub>	1,450	1,260 ± 300		~20,000	1.0	250 ± 25	$\mu$ probable

\* B, P, M, O, K Bristol, Paris, Milan, Oslo, Copenhagen.

ually only when their length is at least of the order of 3,000  $\mu$ .

*Primary mass.*—Mass measurements were made in Paris on the three long (5,000 to 9,500  $\mu$ ) primaries coming from stars, each primary giving two independent values [scattering-range and ionization-range (25)]. There is agreement between the six values, which give:  $M_\kappa = (940 \pm 40) m_e$ .

Note that no  $\kappa$ -meson mass measurement made in other laboratories disagrees with this value. The longest track giving the best measurements are:  $\kappa_{B_2} (1,125 \pm 230)$ ,  $\kappa_{B_{12}} (870 \pm 100)$ ,  $\kappa_{M_2} (1,040 \pm 120)$ , and  $\kappa_{O_1} (950 \pm 140)$ .

One can add to these values the two best recent measurements from the Cornell group (26):  $\kappa_{C_1} (1,020 \pm 150)$ , and  $\kappa_{C_2} (1,000 \pm 200)$ .

Up to the present time, we believe there is no evidence from direct measurements for two different  $\kappa$ -meson masses.

*Secondary spectrum and nature.*—(a)  $\kappa$ -mesons: one can assume the  $\kappa$ -meson of mass  $940 \pm 40$  to be responsible for most of the observed events with the following decay scheme:  $\kappa \rightarrow \mu + 2$  neutral particles. It is then pos-

sible to calculate the maximum energy of the  $\mu$  as a function of the mass of the neutral particle. If they are assumed to be very light (neutrino or photon), one obtains for the maximum energy:

$$p\beta c = 200 \text{ Mev for } M = 940 m_e$$

$$p\beta c = 220 \text{ Mev for } M = 1,000 m_e.$$

As a matter of fact, three secondaries longer than 2,000  $\mu$  were found with a  $p\beta c$  of the order of 250 Mev, larger than the above limits, but there is no true disagreement between these energetic secondaries and these limits.

If another decay scheme is assumed:  $\kappa \rightarrow \mu + \pi^0 + 1 \text{ light neutral particle}$ , the spectrum limit is reduced to  $p\beta c = 180 \text{ Mev}$  for  $M_\kappa = 940$  and 200 Mev for  $M_\kappa = 1,000$ ; that can still be in agreement with the experimental results but it is a little more difficult. Any other decay scheme with more than one neutral particle of mass not smaller than that of the  $\pi^0$  (e.g., a  $\theta_2^0$ ) is excluded because of the small mass value of the primary particle.

To sum up, the Paris group (27) thinks that most of the  $\kappa$ -particles observed till now and stopping in the emulsion can be interpreted as the decay of a particle of mass slightly smaller than or at most equal to 1,000 electronic masses, into three particles, one of them being a  $\mu$ ; the upper limit of the energy spectrum of the  $\mu$  is about  $p\beta c = 200 \text{ Mev.}$ , the sum of the neutral particle masses not being larger than the  $\pi^0$  mass.

(b)  $\chi$ -mesons: it does not look like all the events can be interpreted that way. The four secondary particles which the Bristol group identified very probably as  $\pi$ 's do not fit in these interpretations; they are the B<sub>7</sub>, B<sub>8</sub>, B<sub>9</sub>, and B<sub>17</sub> cases (28). B<sub>9</sub> gives a remarkably long (19,500  $\mu$ ) secondary: one gets  $p\beta c = 179 \pm 18 \text{ Mev}$ , with an ionization equal to  $1.048 \pm 0.025$  times the plateau value. The point is perfectly on the  $\pi$  meson curve. B<sub>8</sub>, with 7,650  $\mu$ , gives almost certainly a  $\pi$ . Nevertheless, the discrimination between  $\pi$ 's and  $\mu$ 's is particularly difficult when the ionization is about that of the plateau and one has to be very careful in drawing conclusions [see Menon's thesis (28)].

So, the  $\chi$ -meson is still very probable, though till now it is impossible to differentiate it from the  $\kappa$ -meson by direct mass measurements. If we therefore assume  $\chi \rightarrow \pi + N^0$ , what can one say about  $N^0$ ? First, the conservation laws, given the  $\pi$ -meson observed  $p\beta c$ , give the following values for the  $\chi$ -mass:  $M_\chi = 915, 990, 1,400$  respectively, if one assumes the  $N^0$ -mass to be that of neutrino,  $\pi^0$ ,  $V^0$ -primary. As the  $N^0$  momentum should be directed opposite to that of the  $\pi$ , one looks in the  $N^0$  direction for a decay or interaction event, but nothing was found for 20,000  $\mu$ .

*Fast heavy meson production.*—We saw that six slow  $\kappa$ -type mesons have been observed coming out from stars. A study has been made in Bristol on fast particles coming out of high-energy stars (29): it was found that heavy mesons, of mass around 1,200, are produced together with  $\pi$ 's. The ratio  $N_\kappa/N_\pi$  of the number of heavy mesons to the number of  $\pi$ 's increases with the incident particle energy; this ratio  $\sim 0.1$  at 10 Bev, but for very high pri-

mary energy ( $\sim 500$  Bev)  $\pi$ 's and heavy mesons would be about equally produced.

### S-EVENTS IN CLOUD CHAMBER

Cloud chamber work yielded evidence for a process which might be closely related with  $\kappa$ -mesons observed in photographic emulsions.

These experiments, which were performed in Rossi's Laboratory at the Massachusetts Institute of Technology, have been published since 1951 (4, 30, 31, 32). In a multi-plate cloud chamber, with plates of  $\frac{1}{4}$  inch lead, triggered by a penetrating shower detector and working at 3,200 m. above sea level, about twenty events of the following kind are observed: a very high ionizing particle comes to rest in one of the lead plates and produces a high-energy secondary particle which can go through several plates without

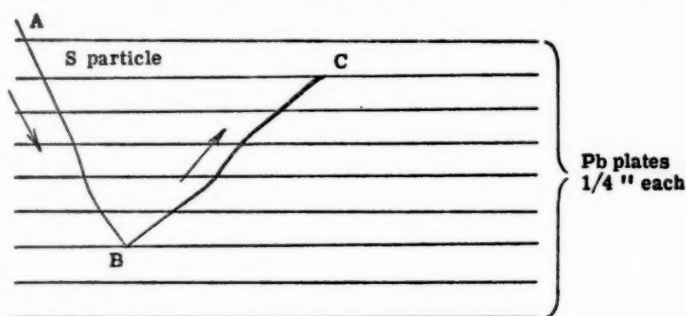


FIG. 2. A typical S-event.

multiplication. The process is shown schematically in Figure 2. AB is the primary particle and BC the ionizing secondary particle. For purely phenomenological reasons the process is named S (for stopping particle), pending further identification.

*Primary mass.*—One can only give an estimate of the mass from scattering in the plates and ionization in-between the plates (rough estimation). The mass is found to be larger than the  $\pi$ 's and compatible with 1,000 to 2,000 electron masses. The authors give 1,470  $\left\{ \begin{array}{l} +410 \\ -360. \end{array} \right.$

*Nature and energy of the ionizing secondary particle.* It is a  $\pi$ - or  $\mu$ -meson. In one event, it stops in one of the plates and the lead thickness which it goes through is 65.6 to 67.7 gm./cm.<sup>2</sup>. In another event it looks like the secondary stops after going through the same thickness, but the evidence is not so clear: if one assumes it is a  $\pi$ , the momentum is then  $213 \pm 2$  Mev/c. In the other events the secondary particle gets out of the illuminated region before going through 60 gm./cm.<sup>2</sup>. No event disagrees with the assumption of monokinetic emission of the secondary, suggesting that the S-primary decays into two bodies, very much like the  $\chi$ -mesons, as can be seen from the secondary momentum value.

This view has been changed recently (33) by the discovery of a longer secondary track: the particle goes through a little over 70 gm./cm.<sup>2</sup> lead, then disappears in the gas. Its momentum value is about 200 Mev/c from scattering through the plates, in case it is a  $\mu$ -meson; on the other hand, one can calculate its minimum momentum value to penetrate the plates and one gets about 200 Mev/c also.

Furthermore, in other events for which it is difficult to draw conclusions, the secondary might stop in a plate with a range much smaller than these values.

As a matter of fact, it is impossible to tell whether the secondary is a  $\pi$  or a  $\mu$ . If it were a  $\mu$ , momentum measurement gives a maximum value of about 200 to 220 Mev/c, which is in agreement with observations made on  $\mu$ -mesons coming out from  $\kappa$ -mesons in photographic emulsions. The secondary might also be a  $\pi$ : there being no nuclear interaction along the secondary tracks is not positively against that, because nuclear interaction might yield heavy particle prongs which are readily absorbed by the lead and escape observation. In fact, no nuclear effect has been observed along the secondary tracks: just a wide-angle single scattering in a plate near the end of the range, which might be a Coulomb scattering. The total secondary track length observed is more than four times the geometric mean free path in lead.

*Emitted neutral particles.*—Observations were made in the opposite direction from that of the secondary, which might tell something about the emitted neutral particle(s). If it is a two-body decay, the ionizing secondary and the neutral particle would be ejected in opposite directions, but that does not imply that one could observe any effect of the latter in the direction opposite to that of the ionizing secondary: for example, if the neutral particle was a  $\pi^0$ , it should very quickly disintegrate into two photons which, from the known  $\pi^0$ -momentum value, would be emitted in the cloud chamber in two directions making an angle of about 60°. These photons would give electron showers in the lead plates, but they should be observed on both sides of the prolongation of the ionizing secondary. On the other hand, in case there is just one emitted photon, one should frequently find a shower along the opposite direction. At first (34), it seemed there were no photons nor  $\pi^0$ -meson as neutral decay product. But recently (33) in three cases, an electron shower was observed in the opposite direction to that of the ionizing secondary, though it should have been observed much more frequently in case the emitted neutral particle is always a photon. Finally, if the neutral particle is a  $V^0$ -primary, as may be suggested by one Pic du Midi picture (cf. *infra*), one should see its decay products coming out from a point lying on prolongation of the ionizing secondary. But nothing was observed on a total length corresponding to a time larger than  $10^{-8}$  sec. So it cannot be the  $V^0$  which is observed in cloud chambers. It is not yet clear as to the character of the neutral particle(s), but the multi-plate cloud chamber is certainly the best apparatus for detecting this (these) neutral particle(s).



*S-primary mean-lifetime.*—The long *S*-primary track length observed in the cloud chamber shows that the mean-lifetime of these particles is quite long. To be stopped, *S*-primaries need a time of  $10^{-9}$  sec., in their reference frame. Their mean-lifetime cannot be much smaller than  $10^{-9}$  sec.

An estimation of this mean-life has been made from the ratio of the number of particles decaying in flight to the number of particles decaying at rest: assuming charged *V*-primaries observed in cloud-chambers are of the same nature as the *S*'s and estimating how many  $V^{\text{ch}}$ -primaries are stopped before decaying, one gets the inequality:  $2 \times 10^{-9}$  sec.  $< \tau_0 < 2 \times 10^{-8}$  sec.

#### CHARGED *V*-EVENTS

Since the first picture was obtained and interpreted by Rochester and Butler in 1947 as the decay in flight of a charged particle heavier than a meson, and confirmed by the Pasadena group (35) and then by other groups (30, 36, 37), progress in the knowledge of  $V^{\text{ch}}$  properties have been rather slow. The observed number (less than a hundred cases as a whole) is much less than the number of neutral *V*-particles and their characteristics not so well known. It is usually difficult to make a good momentum measurement on both tracks for they are almost in a line, and if one is long enough to allow a good measurement then the other is much too short. The secondary track yields generally more information, which requires considerations on transverse momentum that will be developed below.

The main results can be summarized as follows:

*Primary particle.*—In some cases its mass has been estimated to be smaller than the proton mass and in agreement with the mass attributed to  $\kappa$ -mesons in photographic emulsions (38, 39). In a few other cases it is equal to or larger than the proton mass (40). Such types of positive heavy *V*-primaries have been found by the Pasadena group. In fact the primaries are too short to allow accurate mass measurement but the secondaries exhibit much larger masses than  $\pi$ -mesons, and are compatible with the proton mass; on the other hand, the possibility of interpreting such events by the scattering of a proton on one of the argon nuclei of the chamber gas can be excluded. It is natural to suggest that the primary disintegrates into a proton and probably a  $\pi^0$ , very much like the  $V_1^0$  which disintegrates into a proton and a charged  $\pi$ .

Upon examination of the  $V^{\text{ch}}$  distribution in both parts of a cloud chamber separated by a lead plate, one observes that the primary particles seem to divide into two groups of different mean-lifetimes; the group of shorter lifetime would include the superprotons (hyperons *H*).

Let us mention finally that several negatively charged particles of mass intermediate between meson and proton masses have been observed in the cloud chamber, coming from a nuclear interaction of high energy and crossing the chamber without undergoing decay (38, 41); these are most probably  $V^{\text{ch}}$ -primaries: their mass measurement is good on account of the

tracks being rather long. These tracks are included when the  $V^{\text{ch}}$ -primaries mean-lifetime is estimated.

To sum up the  $V^{\text{ch}}$ -properties, the existence of at least two groups of  $V$ -particles seems to be well established: the "light" ones whose mass is similar to the  $\kappa$ - or  $\chi$ -meson mass, including particles of both signs and corresponding to a long lifetime (of the order of  $10^{-9}$  sec); the "heavy" ones or "superprotons" of much shorter mean-lifetime, (of the order of  $10^{-10}$  sec) counterpart of superneutron  $V_1^0$  and decaying into a proton and probably a neutral meson (H-particles).

*Identification of secondaries:* (a) Superproton primaries (H-particles). In the few cases where the superproton primaries have been well identified the visible secondary is likely to be a proton. On the other hand the transverse momentum values measured on these secondary tracks are in good agreement with the ones expected from the following scheme:

$$H^+ \rightarrow P + \pi^0 + Q (\sim 40 \text{ Mev})$$

when the  $Q$ -value is assumed to be of the same order of magnitude as the  $V_1^0$   $Q$ -value. Besides, the alternate decay mode,

$$H^+ \rightarrow N + \pi^+ + Q (\sim 35 \text{ Mev})$$

which seems to have manifested itself in photographic emulsions (42), has not up to now been observed. Such a reaction could not practically be distinguished from  $\kappa$ -meson decay, except in very favorable cases.

(b) Light  $V^{\text{ch}}$ -primaries. There have been several events observed which favour the identification of the secondary as a meson of the  $\pi$  or  $\mu$  type without it being possible generally to differentiate these two particles.

An interesting case was published at Massachusetts Institute of Technology (30), where a slow  $V^{\text{ch}}$  secondary in a lead plate creates a nuclear interaction characterized by a large angle scattering. It is very likely to be a  $\pi$ -meson, its mass being of the order of the meson mass. The case is interesting: it appears as a kind of transition between the  $S$  and the light  $V^{\text{ch}}$  cases since the primary is rather slow; besides, the range of the secondary  $\pi$  is known and gives a lower limit of its momentum in the center-of-mass system of the  $V$ -primary: this lower limit corresponds to the extreme case where no energy is lost during the scattering of the  $\pi$ -meson. The value  $200 \pm 30 \text{ Mev}/c$  is in good agreement with the Bristol results on identified  $\pi$ -mesons among  $\chi$ -mesons secondaries. This lower limit is on the other hand too high to allow identification of the primary with a possible superproton decaying into a neutron and a  $\pi$ -meson, at least as long as the  $Q$  value of this possible reaction is not supposed to exceed 40 Mev.

*Two- or multiple-body decay.*—Apart from these special cases one can try to find out whether two-body or multiple-body decay is involved. In the first case, the momentum of the ionizing particle will always be the same in the primary frame of reference; but not in the second case. To clarify the problem, the method of transverse momentum is used which we now de-



scribe; it is equally useful for the decay products of other particles disintegrating in flight.

*Transverse momentum method (38).*—Let us call 1 and 2, the observable primary and secondary tracks, respectively, and  $\theta$  the angle between them (See Fig. 3). When the primary velocity is known (ionization measurement)

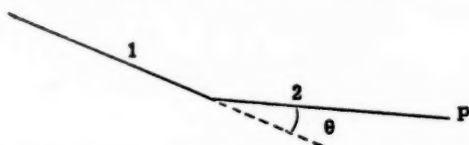


FIG. 3. Primary [1] and secondary [2] tracks in a decay.

together with the momentum of the secondary in the laboratory frame of reference, the momentum of the secondary in the frame of reference of the primary can be computed. Then it will be possible to know, by comparing the results, whether this momentum is always the same; if so, this would establish the two-body decay. Unfortunately, the primary velocity is hardly ever known, though it can sometimes be estimated with greater or lesser reliability. Let us suppose that the secondary momentum value  $P$  is available;  $\theta$  being known,  $P_t = P \sin \theta$  is derived. It is well known that  $P_t$  is conserved through Lorentz transformation from the laboratory frame to the primary frame of reference. If we suppose that the disintegration takes place at random in the primary frame and generates two particles only, the most probable direction of emission is at  $90^\circ$  with the primary particle direction (from elementary solid angle considerations); the least probable is about  $0^\circ$  and  $180^\circ$ ; moreover at  $90^\circ$  we have  $P^* = P_t$  ( $P^*$  being the momentum of the secondary in the center-of-mass system). The curve (Fig. 4) shows the distribution of  $P_t$ . If different  $P_t$  values can be measured in the laboratory

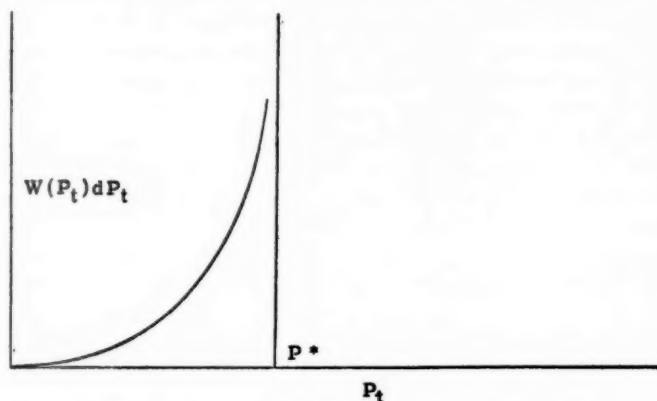


FIG. 4. Distribution of transverse momenta in a two-body decay.

system and their distribution is in agreement with the theoretical curve, then we can be sure of a two-body decay and compute the value of  $P^*$ .

*Results on  $V^{\text{ch}}$  secondaries.*—This plot of transverse momentum distribution was established by the Manchester group but the results are not very precise and rather favor a three-body decay distribution. There may be perhaps superposition of more than one mode of decay, in agreement with the fact that both  $\pi$ - and  $\mu$ -mesons seem to be found among the  $V^{\text{ch}}$  secondaries.

Not much is known about emitted neutral particles: a Manchester picture shows a  $V^{\text{ch}}$  together with a neutral  $V$ , the disposition of tracks suggesting that the neutral  $V$  might be the neutral product of the  $V^{\text{ch}}$ . Unfortunately this picture is not too convincing and is unique.

*$V^{\text{ch}}$ -primary mean-lifetime.*—Following preliminary indications obtained in Manchester, the Pasadena group (40) suggested the existence of at least two mean-life values, of about  $10^{-9}$  and  $10^{-10}$  sec., the latter corresponding to nearly all positive primaries. The evidence was established after results obtained in a cloud chamber with a plate. On the other hand, a systematic study of mean-lifetimes achieved at the Jungfrauoch by the Manchester group (41) established that one at least of the  $V^{\text{ch}}$  types had a mean-life longer than  $4 \cdot 10^{-9}$  sec.

#### NEUTRAL $V$ -EVENTS

Three years after the first event interpreted as the decay in flight of a neutral particle was observed (2), confirmation of the fact was given in a remarkable way by observation of 34 similar cases made by the Pasadena group with a cloud chamber operating in the California mountains (35). Besides, confirmation seems to come also from the observation in a photographic emulsion of a forked track in the vicinity of a large star (43).

In 1951, much information was contributed by different laboratories working at sea level or at mountain altitude (4, 30, 36, 37, 38, 44, 45, 46). The main facts then established were the following:

$V^0$ 's are produced in conjunction with high-energy nuclear interactions. Two ionizing tracks are observed to start from the same point. The Manchester group (38) distinguished two different events corresponding to two kinds of neutral  $V$ 's, for in some cases one of the tracks can be characterized as a proton track whereas in others the proton is excluded.

It now seems established that one of the neutral  $V$ -primary types disintegrates with a proton as positive particle. This type is called  $V_1^0$  (or  $\Lambda^0$ ).

$\Lambda^0$ -particle.—(a) The  $\Lambda^0$  particle is, in some experimental arrangements, the very large majority of particles whose decay is observed. (b) It must be taken as certain that one of the tracks is a proton. It is relatively easily identified in a cloud chamber when its ionization is larger than 2.5 times the minimum. At first, two important questions have to be answered about the secondary: what is the nature of the other ionizing secondary and how many neutral particles are emitted?

A practical and efficient method to obtain information about decay in

flight was developed by the Manchester group and then precisely particularized by Thompson (50). We are going to describe it briefly for it yields interesting elements of knowledge.

*$\alpha$ -parameter method.*—The  $V$ -primary of mass  $M$  is assumed to decay into two bodies only, of masses  $M_1$  and  $M_2$ ; in its own frame of reference, where the  $V$ -primary is at rest, the two particles are emitted with equal and opposite momenta  $P^*$  at an angle  $\theta^*$  with the  $V$ -primary direction.  $P^*$  is then a function of the masses:  $P^* = [M^2 - (M_1 + M_2)^2]^{1/2} [M^2 - (M_1 - M_2)^2]^{1/2} / 2M$  where momenta and masses are expressed in energy units ( $c=1$ ). In fact, measurements carried out in the laboratory frame yield  $P_1$ ,  $P_2$ ,  $\theta_1$ ,  $\theta_2$  (see Fig. 5) in the favorable cases. Let us consider the momentum components  $P_L$

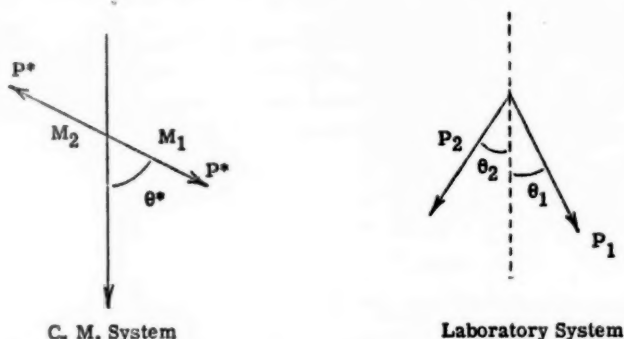


FIG. 5.  $V$ -primary decay in center-of-mass and laboratory systems.

along the  $V$  direction, and the transverse component  $P_t$ . The transverse momentum  $P_t = P_1 \sin \theta_1 = P_2 \sin \theta_2$  is a Lorentz invariant:  $P_t = P^* \sin \theta^*$ . Let us define the quantity:  $\alpha = (P_{1L} - P_{2L}) / P$ ; it can be simply written as follows:

$$\alpha = (M_1^2 - M_2^2) / M^2 + 2P^* \cos \theta^* (M^{-2} + P^{-2})^{1/2} \quad 1.$$

$$\alpha = (P_1^2 - P_2^2) / P^2 \quad 2.$$

$$\alpha = -\sin (\theta_1 - \theta_2) / \sin (\theta_1 + \theta_2) \quad 3.$$

It is clear that for an isotropic decay in the center-of-mass the angle  $\theta^*$  is distributed at random; the mean value of the  $\cos \theta^*$  term is zero and  $\alpha$  is symmetrically distributed about  $(M_1^2 - M_2^2) / M^2$ , the width of the distribution depending on the velocity distribution of the primaries.

Let us suppose that the disintegration products are of equal masses: the  $\alpha$ -values measured either by momenta (formula 2) or by angles (formula 3) will be symmetrically distributed about zero. If the two particles are a proton and a  $\pi$ -meson, the mean value of  $\alpha$  will be  $\bar{\alpha} = 0.69$  in case the  $Q$ -value of the reaction is 40 Mev.

The  $\alpha$ -parameter can be used in many different ways. An interesting attempt is to plot  $\alpha$  as a function of the transverse momentum  $P_t$ . The nature of the distribution of  $P_t$  in the case of a two-body decay has already been pointed out above.

In the center-of-mass system, we have  $P_L^{*2} + P_t^{*2} = P^{*2}$ , and taking relation (a) into account, we find:

$$(\alpha - \bar{\alpha})^2 / (2P^* / \beta M)^2 + P_t^2 / P^{*2} = 1$$

where  $\beta$  is the primary particle velocity in the laboratory frame.

Thus, for a given primary velocity, measurements of  $\alpha$  as a function of  $P_t$  place themselves on an ellipse, which varies according as  $\beta$  varies; however, it can be usually assumed that  $\beta = 1$ . If so, whatever the primary energy, the experimental values must occupy a single ellipse if two-body decay of one type occurs. If the disintegration implies production of a neutral particle (three-body decay), then the observed values should be spread about the ellipse, which then corresponds to zero kinetic energy for the neutral particle in the center-of-mass system.

One can try to see whether the experimental values fit some of the ellipses corresponding to the different mass values and  $Q$ -values considered. Figure 6 shows Thompson's results on a small number of neutral  $V$ -primaries (50). The ellipses correspond to the following cases:

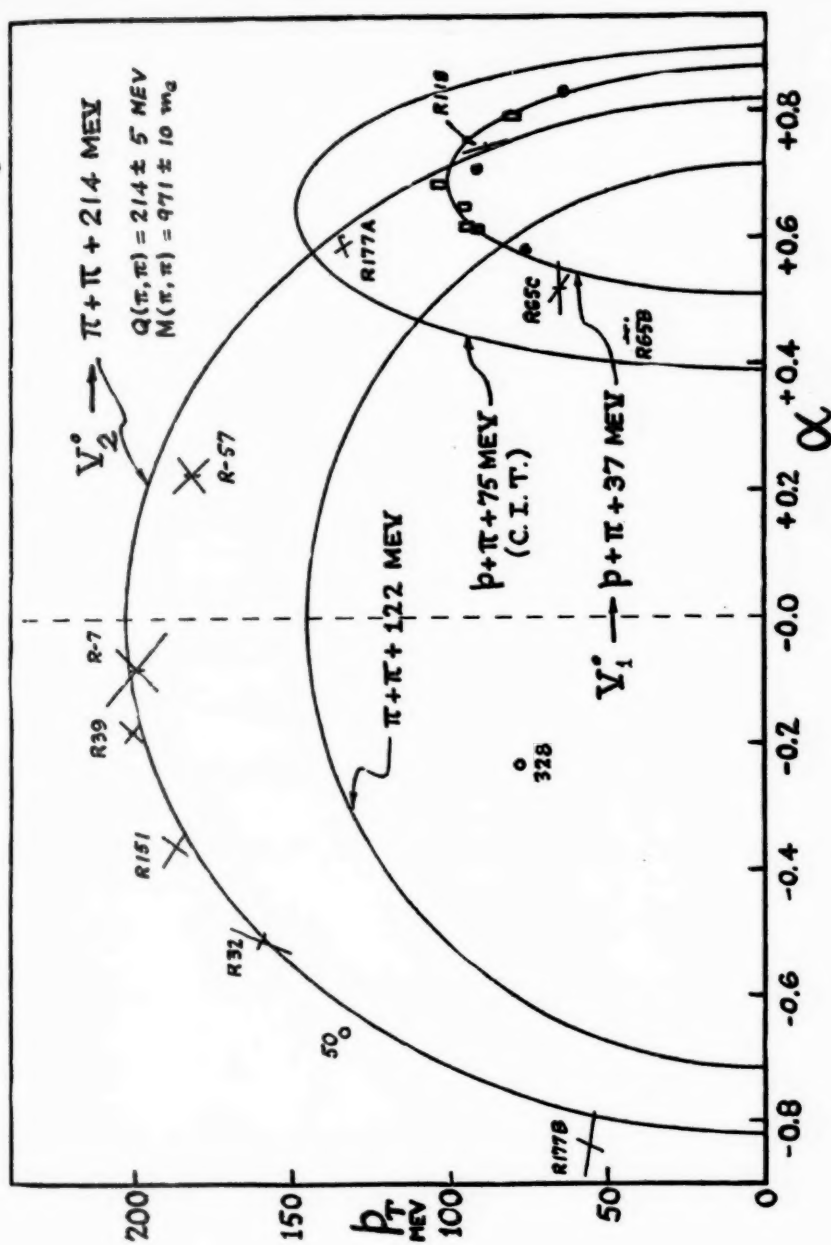
the right end ones to	$\Lambda^0$ (or $V_1^0$ ) $\rightarrow P + \pi + 37$ Mev and
	$\Lambda^0$ (or $V_1^0$ ) $\rightarrow P + \pi + 75$ Mev,
the others to	$\theta^0$ (or $V_2^0$ ) $\rightarrow \pi + \pi + 214$ Mev and
	$\theta^0$ (or $V_2^0$ ) $\rightarrow \pi + \pi + 122$ Mev.

These different modes of decay will be examined below.

*Coplanarity tests.*—We have seen above how knowledge of transverse momentum distribution can distinguish between two- or multiple-body decay; but the results are not always clear. A possible approach to the problem consists in the use of coplanarity tests: one must check whether the plane of the two secondaries contains the primary track direction. The origin of  $V$ -primary is supposed to be known, as is rather often the case: a nuclear interaction observed in a multi-plate cloud chamber must sometimes be considered as having generated the  $V$ -primary whose decay products are visible. But this is not always certain, and much care is required to obtain a well defined  $V$ -primary path.

Let us suppose that the path is defined; the deviation from coplanarity, or the angle between the  $V^0$ -path and the plane of the two decay tracks is called  $\delta$ . It is clear that  $\delta$  is not an adequate variable for discussion of the possibility of three-body decay. Because if the  $V^0$ -particle is very fast,  $\delta$  will still be small, all the decay products being then projected forward in the laboratory frame, the angles being smaller for larger  $V$ -primary energy.

It is easily seen that an adequate variable to be studied is  $\beta\gamma\delta$ ,  $\beta$  being the  $V$ -primary velocity and  $\gamma = (1 - \beta^2)^{-1/2}$ ; the factor  $\beta\gamma$  is the reduced momentum  $P/Mc$  of the  $V^0$ -primary. Unfortunately  $\beta\gamma$  cannot be computed, for it can only be deduced from experimental data on the two visible secondary particles; but it depends of course on the possible neutral product. This is not too serious, for the neutral particle is generally not supposed to be

FIG. 6. Transverse momentum plotted against the  $\alpha$ -parameter.

heavier than a  $\pi^0$ , and then its longitudinal momentum is on the average not larger than that of the visible meson. In fact, what is more important in the  $\beta\gamma$  determination is the longitudinal momentum of the proton in the case of the  $V_1^0$ .

Thus, the variable  $\beta\gamma\delta$  is computed in each case,  $\delta$  being an angle measured in space when the  $V$ -primary origin is known, and  $\beta\gamma$  being the reduced primary momentum estimated through measurements of both visible secondary tracks. Indeed, these measurements involve some inaccuracy, the cause of which will not be discussed here. Then the curve giving the number of events versus each  $\beta\gamma\delta$ -value is plotted. If a two body distribution is implied, the curve will be very sharp about the origin; in the case of three-body decay, the curve should fall off smoothly on both sides.

*Coplanarity test in the case of  $V_1^0$ -events.*—Figure 7 shows results obtained on  $V_1^0$  at Massachusetts Institute of Technology and what should theoretically be obtained for a three-body decay (49). Some small values of  $\delta$  can indeed be found and might well come from small errors in the reconstitution of the events. One can see that this result provides very strong evidence in favor of the two-body decay of the  $V_1^0$  primary. It must be pointed out that the Pasadena group does not find such significant evidence (47).

*Nature of the negative particle coming from  $V_1^0$ -decay.*—Its  $\pi$ -meson nature

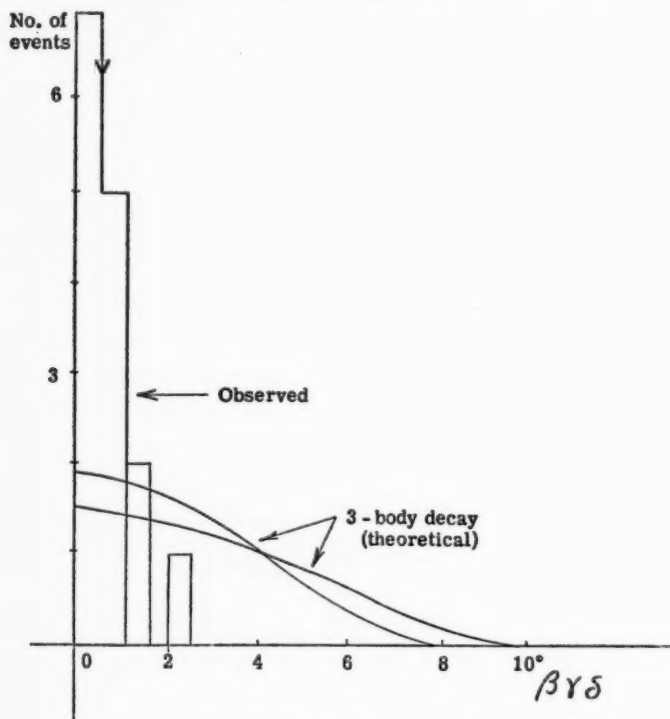


FIG. 7. Test of coplanarity.

seems to be established. Comparison of the proton and the negative particle momentum leads to this conclusion; moreover, in some cases this particle undergoes  $\pi-\mu$  decay or a nuclear interaction. Further, the mean free path for nuclear interaction measured on this particle is not far from the geometrical value. All this evidence shows that a  $\pi$ - rather than a  $\mu$ -meson is implied. The latter would only be present in very small proportion among the  $V_1^0$  secondaries.

*Conclusions about the  $V_1^0$ .*—To sum up, there are the following conclusions: (a) The two ionizing particles are a proton and a  $\pi$ -meson (all authors agree on this). (b) All groups are also in agreement in admitting a two-body decay, at least in a very large majority of the events. (c) All groups, except the Pasadena group, agree to admit a single  $Q$ -value:  $Q=38\pm 1$  Mev; we would then have:  $V_1^0 \rightarrow P + \pi + (38\pm 1)\text{Mev}$ .

The Pasadena group results are not in agreement with this value. They find the  $Q$ -values to lie between 10 and 100 Mev, nearly all of the values clustering around two discrete values, viz.  $35\pm 3$  and  $75\pm 5$  Mev (47).

*Observation of nuclear fragments containing  $V_1^0$ 's.*—In a few cosmic rays stars observed in photographic emulsions, it looks as if one of the heavy fragments emitted from the star ( $Z$  between 3 and 6) contains a  $V_1^0$  (51, 52, 53). One sees originating from the end of the fragment a small star which can be interpreted as made by the decay of a  $V_1^0$  included in the fragment. In one of the events (53) the process is consistent with the emission of a proton, a  $\pi$ -meson and a recoil nucleus according to:  ${}^7\text{Li}^* \rightarrow {}^6\text{Li} + P + \pi^- + (28\pm 4)$  Mev which is in agreement with:  $V_1^0 \rightarrow P + \pi + (35\pm 4)$  Mev if one assumes the  $V_1^0$  binding energy in the lithium fragment to be that of a neutron.

#### NEUTRAL $V$ -EVENTS ATTRIBUTED TO $K$ -MESONS

It seems certain that there are  $V^0$ 's for which the positive decay particle is lighter than a proton. An event which can be regarded as a decay in flight of a neutral particle into two  $\pi$ - or  $\mu$ -mesons is named  $V_2^0$ . Decay particles look lighter than a proton and the  $\alpha$  parameter is symmetrically distributed around zero, indicating about the same mass value for the two particles. In several cases it is very probable there is no emitted neutral particle; it is certain that one of the particles is a  $\pi$  and the other is a  $\pi$ - or a  $\mu$ -meson.

The question of the  $Q$ -value is not settled: the first values were very much spread around 120 Mev (44). They seem to get closer to the value  $Q=210$  found by Thompson with a small number of very good events (50), but there still exist possible smaller values: at M.I.T. four events whose best interpretation is a decay into two  $\pi$ 's give  $Q$ -values between 75 and 200 Mev.

#### OTHER $V^0$ -EVENTS

Very probably there are other types of  $V^0$ 's for which the negative particle is heavier than  $\pi$ - or  $\mu$ -mesons (47). Not much is known yet as only a few examples have been found.

*Mean-lifetime measurements.*—Let us assume we know the time  $t_i$  that



elapses between the production and decay of each  $V$ -primary. If the number  $N$  of  $V$ -primaries is large, the mean-lifetime will be:  $\tau = \sum t_i / N$  provided  $t_i$  is measured in the particle frame of reference and not in the laboratory frame. We know the distance  $D$  between the production and decay of the  $V$ . If furthermore we know the velocity  $\beta c$  we get:  $t_i = D\sqrt{1-\beta^2}/\beta c$ . For example, one can measure  $D$  when one knows the starting point and observes the decay; sometimes one can estimate  $\beta$  from the dynamical characteristics of the secondaries with an assumption about the mode of decay.

Unfortunately, there is a number of corrections: indeed, we do not observe decays occurring before entering the chamber, and after leaving the chamber. Furthermore, decays occurring in the chamber plates are lost. These important corrections yield a more complex relation. The latest results are:

$$\begin{array}{ll} \tau^0 = (2.5 \pm 0.7) 10^{-10} \text{ sec} & (47) \\ \text{for the } V_1^0 \left\{ \begin{array}{l} \tau^0 = (10 \pm 7) 10^{-10} \text{ sec} \\ \tau^0 = (3.5 \pm 1.2) 10^{-10} \text{ sec} \end{array} \right. & (48) \\ \text{for the } V_2^0 \quad \tau^0 = (4 \pm 3) 10^{-10} \text{ sec} & (49) \end{array}$$

## PRINCIPAL EXPERIMENTAL FACTS PRESENTED AT THE BAGNÈRES CONGRESS<sup>2</sup>

### $\tau$ -MESONS

An important contribution has been furnished by the group at Bombay (56) thanks to the utilization of stripped emulsions irradiated in sounding-balloons: three new  $\tau$ -mesons have been identified. The principal results are the following: (a) Assuming the process  $\tau \rightarrow 3\pi$ , the mass is

$$\begin{aligned} M_\tau &= (969.3 \pm 1.7)m_e \quad \text{with} \quad M_\pi = 276m_e \\ Q &= 72.2 \pm 0.8 \text{ Mev} \end{aligned}$$

(b) Five of the light mesons observed, out of the nine created by the  $\tau$ -mesons, stop in the emulsion; these are  $\pi$ -mesons. For one of the  $\tau$ 's, two of the three created  $\pi$ 's stop (they are positives) in another case, one of the observed  $\pi$ 's is negative. (c) If all the results obtained on  $\tau$ -mesons in the different laboratories are considered, one may deduce that eleven  $\pi$ 's have been observed terminating in the emulsion; there is no evidence in favor of  $\mu$ 's. Of the eleven  $\pi$ 's, eight are positive and three are negative: this proportion is compatible with the hypothesis that all  $\tau$ 's disintegrating into three mesons at rest are positive. (d) If they are assumed to be positive  $\tau$ -mesons and if they are compared with the positive  $\pi$ -mesons stopping within the emulsion, one finds (Bombay) the following ratio:

$$\frac{\text{Slow } \tau^+}{\text{Slow } \pi^+} = (1.3 \pm 0.8)/100$$

<sup>2</sup> They pertain to verbal communications and not to publications. The information thus furnished is not binding upon the authors cited.



(e) Besides the contribution of Bombay, a new  $\pi$ -meson has been observed at Rome (57) compatible with the values given above for  $M_\pi$  and for  $Q$ .

In conclusion, the evidence that  $\tau$ -mesons give three  $\pi$ 's appears to be very convincing. In addition to this result, it seems that only positive  $\tau$ -mesons at rest give three  $\pi$ 's.

#### K TYPE MESONS STOPPING IN EMULSIONS (EXCLUDING $\tau$ 's)

A number of new results on  $\kappa$ -type mesons stopping in emulsions has been presented by the Bristol, Bombay, Brussels, Milan, and Cornell groups (56 to 63). (a) Table III summarizes the data on the new  $\kappa$ -type mesons. Note that the three last ones of Bristol and all those from Bombay have been observed in stripped emulsions with quite long track lengths. (b) With the use

TABLE III

NEW  $\kappa$ -TYPE MESONS (EXCLUDING  $\tau$ -MESONS) STOPPING IN EMULSIONS  
(Presented at the Congress of Bagnères, July, 1953)

Origin	Primary		Secondary				Remarks
	Length In Microns	Mass In $m_e$	Length In Microns	Ionization Relative to Minimum	$p\beta c$ Mev	Type; Mass in $m_e$	
Bristol	1,850	$\sim 1,500$	4,000	$\sim 1.0$	$315 \pm 40$	—	ejected from star ejected from star ejected from star
	6,670	$990 \pm 150$	190	$\sim 1$	—	—	
	350	—	18,000	$0.93 \pm 0$ or	$205 \pm 15$	$\mu$	
	28,000	$780 \pm 90$	6,000	$1.09 \pm 0.04$	$170 \pm 20$	$\pi; 280 \pm 20$	
	7,560	$990 \pm 150$	$500 \times 6$	—	—	—	
	8,560	$1,240 \pm 100$	$3,000 \times 18$	1.2 to 1.5	$119 \pm 9$	$\mu; 203 \pm 8$	
Bombay	13,600	$980 \pm 150$	—	—	$226 \pm 20$	—	ejected from star ejected from star
	12,000	$890 \pm 200$	—	.98	—	—	
	52,000	$970 \pm 150$	—	1.0	—	—	
	31,000	$1,030 \pm 170$	—	.93 $\pm$ .907	—	—	
Brussels	1,400	$1,030 \pm 260$	—	—	—	—	
	2,000	$450 \pm 170$	—	—	—	—	
	3,000	$800 \pm 160$	—	—	—	—	
	20,000	$1,100 \pm 100$	5,000	1.09	$200 \pm 30$	—	
Milan	1,470	$1,340 \pm 400$	2,500	$1.06 \pm 0.04$	$200 \pm 33$	$300 \pm 50$	
	3,400	$975 \pm 155$	290	—	—	—	

of stripped emulsions, it was often possible to follow the track of the  $\kappa$ -meson from the end to its origin: thus five new  $\kappa$ 's coming out of stars were observed. (c) The mass of the primaries, obtained by taking the weighted average of all the measurements on the 33 longest tracks is:  $M_\kappa = 990m_e$ . In 21 cases the standard deviation of the measurement includes the number 990; in 11 cases 990 is within one or two standard deviations. In one case, this value lies outside of two standard deviations. This means that all the mass measurements are not incompatible with one single value of the mass and

that the introduction of two different masses is not required by the direct measurements on the primaries coming to rest. For primaries having track lengths greater than  $3000\mu$  the mass values are:

Average of the Type  $\kappa$  of Bristol:

$$M_{\kappa} = 1060 \pm 35 m_e$$

Average of the Type  $\kappa$  (Bristol excluded):

$$M_{\kappa} = 965 \pm 26 m_e$$

Average of the Type  $\kappa$  of Bristol coming out of stars:

$$M_{\kappa} = 1000 \pm 60 m_e$$

Average of the Type  $\kappa$  coming out of stars (Bristol excluded):

$$M_{\kappa} = 952 \pm 30 m_e$$

(d) Among the secondaries, the existence of  $\mu$ -mesons is confirmed (see in particular the third and last one of Bristol) and the continuous character of the  $\mu$ -meson spectrum is equally well confirmed. Moreover, the existence of the  $\pi$ -mesons seems to be confirmed by several new cases (see the fourth one of Bristol). However, there appears to be no noticeable difference of mass between the type  $\kappa$ -mesons producing  $\mu$ 's and type  $\chi$ -mesons giving  $\pi$ 's. In conclusion, the existence of the  $\kappa$ -meson remains practically certain, that of the  $\chi$ -meson remains probable, but the masses of the primaries differ very little from each other; the direct measurements on the stopped  $\kappa$ -mesons give an average value of the mass between 950 and 1,000. (e) The momentum of the secondary mesons produced by the  $\kappa$ 's seems in a few cases to be higher than the value  $p = 236 \text{ Mev}/c$ . As it may be recalled, this is the value corresponding to the maximum momentum possible for a  $\mu$ -meson emitted in the decay of a particle with the same mass as the  $\tau$  and producing  $\mu + 2$  neutral particles of zero mass. (f) We indicated previously that mass measurements by the Bristol group on heavy and fast mesons emitted by stars give a mass of the order of magnitude of  $1,200 m_e$ . Control measurements applied to protons and  $\pi$ -mesons confirmed these observations (64): it seems to be impossible to lower the above found value to the neighborhood of 1,000. It is very difficult to interpret these well established and soundly based results. On the one hand, they are incompatible with the masses of type  $\kappa$ -mesons stopped in emulsions; on the other hand they do not agree with the masses measured by the École Polytechnique (Paris), in the Wilson cloud chamber or with the primaries of S-events having momenta of the same order ( $\sim 500 \text{ Mev}/c$ ).

#### S-EVENTS OBSERVED IN CLOUD CHAMBERS

(a) Besides the data collected at Massachusetts Institute of Technology (65) new results have been obtained by the Paris group (École Polytechnique) with the help of two big Wilson cloud chambers superimposed upon each other, of 200 liters each, installed on Pic du Midi and in operation now for several months (66). The observed tracks in the upper chamber are bent by a magnetic field and those of the lower chamber have to pass through a number of layers of carbon and lead. The sign of the charge and the mass of the particles stopping in the lower chamber is obtained by measuring their

momenta and ranges. The chamber is triggered by penetrating showers activating the counter. During one day, 150 exposures can be taken; of these, half show nuclear interaction. In particular, four heavy mesons have been observed stopping in the lower chamber; all of them are positive. One with the mass (in units of  $m_e$ ) of  $965 \pm 50$ , is perhaps a  $\tau$ , the other three are type  $\kappa$ - or  $\chi$ -mesons; they give the following masses:  $915 \pm 80$ ;  $1,030 \pm 85$ ;  $885 \pm 50$ . The average of these three numbers is  $922 \pm 40$ . The accuracy and the precision of the measurements have been checked on 20 protons, observed under the same conditions, for which the measured proton mass was  $1827 \pm 35$ . It should be mentioned that if the particles are considered identical with the observed type  $\kappa$ -mesons stopping in emulsions, then the relatively small mass of the latter is confirmed by our measurements on the  $S$ -events. (b) The extension of the observations at Massachusetts Institute of Technology on the  $S$ -event in cloud chambers (20 events) (65) gives  $M_S = (1,200 \pm 270 m_e)$  as average value by scattering and range measurements. The distribution of the scattering variable, for 15 cases where the particles stopped after traversing four or more plates, was found to be consistent with a single mass of about  $1,000 m_e$ . (c) The Massachusetts Institute of Technology group does not find any evidence for the presence of  $\pi$ -mesons among the decay products of type  $\kappa$ -mesons at rest in cloud chambers. The presence of such particles, however, is not ruled out. (d) The Massachusetts Institute of Technology group confirmed the observation that the secondaries of the  $S$ -events do not consist of a group of monoenergetic particles. The momentum of the secondary with the longest range is  $p > 210 \text{ Mev}/c$ , if it is a  $\mu$ -meson. (e) the M.I.T. group confirmed the existence of four cases in which the  $S$ -events give rise to a photon of an apparent energy of the order of 100 to 200 Mev; the direction of the photon is opposite to that of the charged decay product within the experimental uncertainty. However, it is certain that photons with energy equal to or greater than 150 Mev are not associated with all of the  $S$ -events. (f) The primaries of the  $S$ -events observed in the Wilson chambers at M.I.T. and the École Polytechnique have lifetimes longer than  $10^{-9}$  sec.

#### NUCLEAR INTERACTION OF NEGATIVE HEAVY MESONS STOPPING IN EMULSIONS

This problem was not discussed in the first part of this report because of the not completely convincing character of the experimental evidence previously available. In the first indication (Paris, École Polytechnique, 1948), an event obtained with the emulsion C2 (54), a heavy meson directs itself towards the center of a star, from which also emerge several ionizing particles (protons, etc.) and a slow negative  $\pi$ -meson (the latter gives a characteristic star at the end of its track. The energy balance of the star, taking into account the creation of the mass of the  $\pi$ -meson, gives at least 400 Mev. Therefore, if the heavy meson is responsible for the star, it has a mass greater than  $750 m_e$ . However, it must be admitted that the end point of the range of the incident particle is not exactly known because of the existence of a short

track of the star nearly along the direction of prolongation of the primary. Nevertheless, this event has been selected on the basis of two essential criteria: the sense of direction of the particle path considered as having produced the star and the energy balance of the star.

Four or five more recent events seem to confirm this effect (55) of nuclear absorption of heavy negative mesons at rest by nuclei in the emulsion, but none of the cases has been entirely convincing.

At Bagnères a very important confirmation was supplied by the Bombay group (56) thanks to the use of stripped emulsions. Four cases have been observed: in two cases a heavy meson leaves a star, comes to rest in the emulsion and produces a star without a  $\pi$ -meson; the mass of the heavy meson is measured directly ( $1,010 \pm 150$  and  $840 \pm 20$ ). In two more cases an emission of a  $\pi$  out of the star takes place; this brings the event closer to the one cited above.

On the other hand, the Bristol group (67) in a systematic research on G5 plates of  $600 \mu$  has not been able to find any evidence of a nuclear interaction of a heavy meson at rest. Their frequency of events seems to be much more than that of the  $\kappa$  and  $\chi$ -mesons and consequently at least comparable to the rate of the  $\tau$ -mesons at rest giving three  $\pi$ 's. If the total of this evidence were confirmed in the future, it would be concluded that positive or negative  $\kappa$ -mesons never interact at rest with a nucleus; yet  $\kappa$ -mesons do not have an integral spin, if current views are correct (68).

#### CHARGED AND NEUTRAL V-EVENTS

For the moment we will not consider the  $V$ -events attributable to particles heavier than the nucleon (hyperons) and will deal only with the  $V$ -events produced by mesons of mass smaller than nucleons (charged and neutral  $V$ -events attributable to  $\kappa$ -type mesons).

*Charged V-events attributable to  $\kappa$ -mesons.*—(a) For the primary, there is little new evidence: the mass is  $\sim 1,000 m_e$ . (b) The nature of the secondary is given by the following facts: if all of the secondaries are of the same nature it is more probable that they are  $\mu$ 's rather than  $\pi$ 's. The École Polytechnique group (Paris) (66) has indeed observed a collision length of 1.8 in lead and carbon without any nuclear interaction involving the secondaries, but there exists no evidence that all of the secondaries should be of the same nature; the presence of a weak proportion of  $\pi$ 's is not excluded. The Manchester group has described a case where a nuclear interaction of a secondary is probable, but the picture does not seem to be convincing (69). (c) The spectrum of the secondaries indicates that they are not a monoenergetic group. The momentum-distribution is consistent either with a two-body or a three-body decay and the value of the transverse momenta may approach about  $p_\perp \sim 250 \text{ Mev}/c$  (Manchester and the École Polytechnique, Paris). In two cases (one in Manchester and one at the École Polytechnique) it was possible to obtain the value of the momentum of the secondary in the rest system of the primary particle. The values found were:  $p^* = 120 \pm 30$  and  $\sim 100 \text{ Mev}/c$ . These values, smaller than the largest measured values of

transverse momenta, show clearly that secondaries of charged  $V$ -events do not belong to a single monoenergetic group.

*Neutral  $V$ -events attributable to  $K$ -mesons  $\theta^0$  (or  $V_2^0$ ).*—The decay scheme proposed by the Manchester group with the value of  $Q$  specified by Thomson  $\theta^0$  (or  $V_2^0$ )  $\rightarrow \pi + \pi + 214 \pm 5$  Mev has been confirmed, giving a mass  $M = (971 \pm 10) m_e$ , identical to the mass of the  $\tau$  (70, 71). Certain secondaries of this  $\theta^0$  have been observed producing a nuclear reaction in the screens of Wilson chambers (École Polytechnique and Princeton). Analysis of the data of the École Polytechnique has shown that the scheme  $\pi, \pi$  is more probable than  $\pi, \mu$ .

Some small  $Q$  values incompatible with the value of 214 Mev have been presented by such groups as those from California Institute of Technology, University of Manchester, Princeton, University of Indiana (thirteen total cases; seven of these from California Institute of Technology). These values lie between 40 and 130 Mev (70, 72, 73).

The Massachusetts Institute of Technology group fixes the average life-time of  $V_2^0$  at:

$$t_0 = \left(0.9 \pm \frac{1.0}{0.3}\right) 10^{-10} \text{ sec. (75, 76)}$$

#### SUPERNUCLEONS, HYPERONS

*The  $V_1^0$ .*—The scheme  $V_1^0 \rightarrow P + \pi + 37 \pm 2$  Mev has been confirmed by new observations (Massachusetts Institute of Technology, École Polytechnique, Univ. of Rome, Univ. of Milan, Univ. of Manchester, and Tata Inst. Fundamental Research). All of the  $Q$  values are compatible with this value, the precision of the measurement in certain cases being 3 Mev (56, 66, 75, 77, 78). The  $Q$  values found by California Institute of Technology are in disagreement and vary from  $10 \pm 3$  to  $85 \pm 3$  Mev.

Further, an event observed in a cloud chamber (Paris, École Polytechnique) (66) furnishes direct proof that the  $V_1^0$ 's are created out of a pre-existent nucleon and not out of energy. The experiments of Chicago give evidence for the creation of  $V_1^0$  by  $\pi$ 's of low-energy; these results are confirmed by Brookhaven.

If one combines the values of the Massachusetts Institute of Technology, Manchester, 1953, and the low  $Q$  values of the California Institute of Technology, one finds for the average lifetime

$$t_0 = \left(3.3 \pm \frac{0.9}{0.5}\right) 10^{-10} \text{ sec.}$$

*The super protons ( $H^\pm$ -particles).*—The reaction  $V^\pm \rightarrow n + \pi^\pm$  is confirmed by four events (Milan, Genoa, Padua and Bombay) (56, 60, 79) giving  $Q \sim 120$  Mev. The case observed by Bridge and Annis at Massachusetts Institute of Technology is described above. In this latter event the emitted  $\pi$  has an energy of this order. Perhaps this reaction has to be considered as the decay of a super proton inasmuch as the half-life of the heavy particle in the Wilson chamber is only  $3 \times 10^{-10}$  sec.

The reaction  $H^+ \rightarrow P^+ + (\pi^0)$  has been suggested in connection with certain cases, but the evidence is less conclusive than for the above-mentioned reaction (60, 66, 72).

*Cascade of V-events.*—In addition to the cascade of *V*-events observed by the Manchester group (mentioned in the first part of this report) three remarkable new cases have been presented by the California Institute of Technology (72), in which a charged *V*-event is followed by a neutral *V*-event. In four cases the sign of the primary is known to be negative. The scheme  $H^- \rightarrow V_1^0 + \pi^-$  seems the best one for the explanation of these remarkable phenomena.

## APPENDIX ON NOMENCLATURE<sup>3</sup>

### GROUPS OF PARTICLES

1. L-mesons (Symbol L):  $\pi$ -mesons,  $\mu$ -mesons, any other possible lighter meson.
2. K-Mesons (Symbol K): particles with mass intermediate between those of the  $\pi$ -meson and the nucleon.
3. H-particles; Hyperons (Symbol H): particles with mass intermediate between those of the nucleon and the deuteron. This definition to be revised if "fundamental" particles heavier than the deuteron are found.

### PHENOMENOLOGICAL DESCRIPTION

1. *V*-event: Phenomenon which can be interpreted as the decay in flight of a K-meson or a hyperon. Subclasses  $V^0$  and  $V^\pm$ .
2. *S*-event: Phenomenon which can be interpreted as the decay or the nucleon capture of a K-meson or a hyperon at rest.

### INDIVIDUAL NAMES

1. Use small greek letters for mesons. Use capital greek letters for hyperons.
2. Heavy mesons: The most probable are:

$\tau \rightarrow 3\pi$  (certain)

$\kappa \rightarrow \mu + 2$  neutral particles (very probable; nature of neutral particles still uncertain)

$\chi \rightarrow \pi +$  neutral (probable; nature of neutral particle undetermined)

$\theta^0$  (or  $V_2^0$ )  $\rightarrow \pi + (\pi \text{ or } \mu) + Q$  (200 Mev; very probable)

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# EXTRANUCLEAR INTERACTIONS OF ELECTRONS AND GAMMA RAYS<sup>1</sup>

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## INTRODUCTION

The extranuclear interactions of electrons and gamma rays are discussed in nearly all text books on nuclear physics and in some specialized treatises (1, 2). Recently an extensive and critical discussion of both experimental and theoretical work has been given by Bethe & Ashkin (3). Our purpose here is to review the experimental work of the past few years, including enough background theory to give the experiments perspective. Our emphasis is on the work at higher energies. Limited space forces us to omit several topics which might logically be included.

Although there are no important modifications in the basic theory of the interactions, more accurate calculations and improved experimental work have made it possible to compare experiment and theory with some precision. It will be seen that the experimental results are explained by the theory in most cases, although a few discrepancies remain.

## NUCLEAR SCATTERING OF ELECTRONS

The calculation of the scattering of electrons by nuclei has been extended by McKinley & Feshbach (4) and by Feshbach (5) to include a number of elements and a number of energies above 1 Mev. For low atomic number they obtain the following expression for the differential cross section:

$$\sigma = \sigma_R \left[ 1 - \beta^2 \sin^2 \frac{\theta}{2} + \frac{\pi Z \beta}{137} \sin \frac{\theta}{2} \left( 1 - \sin \frac{\theta}{2} \right) \right] \quad 1.$$

where

$$\sigma_R = \left( \frac{Ze^2}{2pv} \right)^2 \csc^4 \frac{\theta}{2}$$

is the Rutherford cross section. This expression represents the cross section very well for  $Z < 13$ . The most accurate calculation for a high  $Z$  element at intermediate energies is that of Bartlett & Watson (6) for Hg. Accurate calculations for a number of elements in the approximation that  $\beta = 1$  are listed by Feshbach (5). These calculations should represent the scattering of electrons of any energy above 4 Mev by a point nucleus.

Measurements by Paul & Reich (7) at 2 Mev and by Kinzinger & Bothe

<sup>1</sup> The survey of the literature pertaining to this [review] was completed in February, 1953.

(8) at 0.245 Mev agree with the calculations for Al but deviate significantly from the calculations for Au at angles above 90 degrees. The results of Paul and Reich, which should be free from screening effects, show a scattering at  $120^\circ$  which is 20 per cent less than that calculated. The reason for this discrepancy is not clear and could be attributed to experimental difficulties. It may, however, indicate that some interaction, which is not included in the calculation, becomes important at large angles.

Corrections attributed to multiple and plural scattering have always been troublesome in these measurements and have been studied experimentally by Reich (9). Although the observed plural scattering has not been explained quantitatively it does not seem that this remains a major source of error. These errors are also discussed by Lipkin (10) in connection with positron scattering.

In experiments discriminating strongly against the detection of electrons that have lost energy in the process of scattering, it is important to correct for the radiation losses which accompany all scattering. This correction can be obtained from a calculation of Schwinger (11) which accounts for this effect in the Born approximation.

The observation of an anomalously large number of  $\delta$  rays accompanying the large angle scattering of slow  $\mu$  mesons in photographic emulsions suggests that such effects may also accompany the large angle scattering of electrons. Ebel & Fry (12) account for this observation by the fact that large angle scattering takes place in regions close to the nucleus where the electron density is high.

#### NUCLEAR SCATTERING OF POSITRONS

The scattering of positrons by nuclei is obtained to a first approximation by replacing  $Z$  in the last term of equation 1. by  $-Z$ . This reduces the scattering of positrons as compared to electrons. The calculation equivalent to that of McKinley and Feshbach has been carried out for 1, 2, 5, and 10 Mev positrons by Yadov (13). That for  $\beta=1$  is included in the calculations by Feshbach (5). These results are shown in Figure 1. Gunnersen (14) has recalculated the scattering of 1.07 Mev positrons and electrons from Hg ( $Z=80$ ) for the case of a screened field and does not find large deviations from that for the simple Coulomb potential.

Cloud chamber experiments on the scattering of positrons (15, 16, 17) have been reported which agree qualitatively with the theory, but in all cases the number of positrons scattered through large angles was too small to show any definite difference from the scattering of electrons.

The only conclusive experiment on the scattering of positrons is that of Lipkin (10) in which the scattering of electrons and positrons of about 1 Mev is compared. The experiment was arranged to observe the electrons and positrons after they had been scattered through 60 degrees by various materials. The observed ratios of the scattering of 1.08 Mev particles by Cu and Pt were 0.52 and 0.31 respectively as compared to theoretical values of

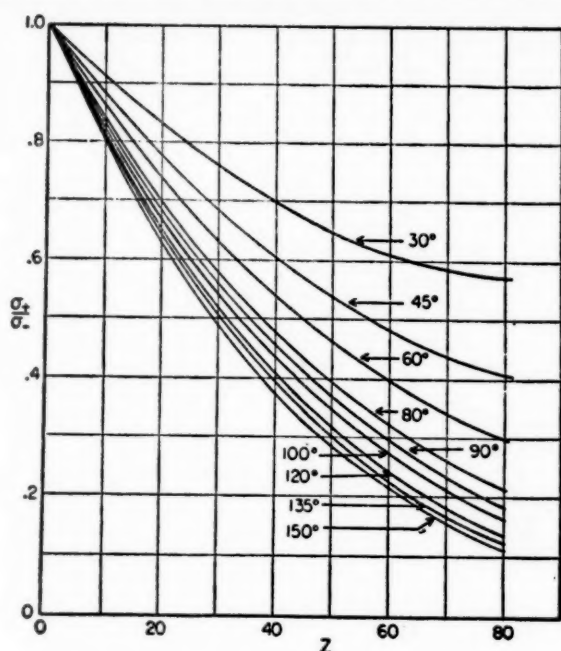


FIG. 1. The ratio of positron to electron scattering by nuclei, for  $\beta=1$ . From Feshbach (5).

0.67 and 0.33. The agreement in the case of Pt, where the effect is large, is remarkably good.

#### EFFECT OF NUCLEAR SIZE

With higher energy electrons now available the electron wave lengths can be of the same order or even much smaller than the nuclear radius. The scattering of such electrons must be described in terms of fields which are not Coulombian at distances less than the nuclear radius. Calculations of the scattering of electrons by charge distributions having a finite size, have been made by Elton (18) and Acheson (19) who show that, in the case of wave lengths of the same order as the nuclear radius, only the  $S$  wave of the interaction is appreciably modified. In this case the deviation from Coulomb scattering can be expressed in terms of a single parameter relating to the charge distribution in the nucleus, namely the volume integral of the perturbing potential [Feshbach (20)]. The effect of nuclear size has been shown to be smaller for positrons [Elton & Parker (20a)].

Experiments on the scattering of 15.7 Mev electrons from a betatron have been reported by Lyman, Hanson & Scott (21). The ratios of observed to Coulomb scattering are shown in Figure 2. The solid lines in this figure represent the calculated reduction in the scattering for uniform charge

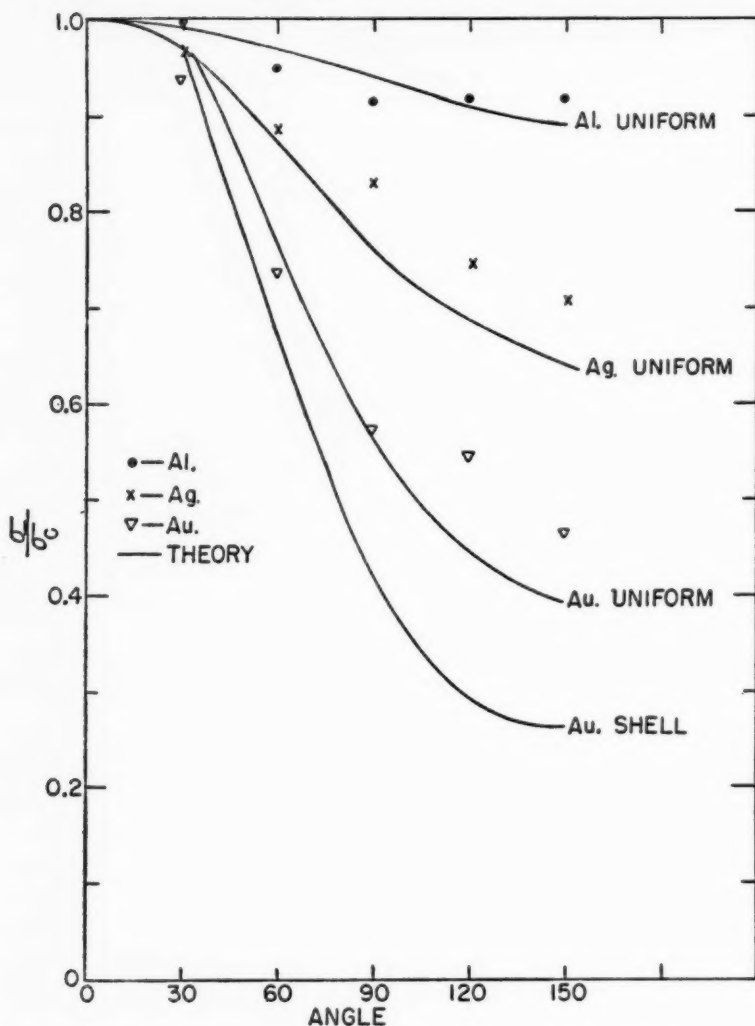


FIG. 2. The ratio of observed to Coulomb scattering of 15.7 Mev electrons by nuclei. From Lyman *et al.* (21).

distributions extending out to radii given by  $R = 1.45 A^{1/3} 10^{-13}$  cm. In the case of Au the lower curve represents the result where the charge is all on the surface of the nucleus. Similar results have been reported by Hammer, Raka & Pidd (22).

At still higher energies it is expected that the scattering will be sensitive to further details of the charge distribution. Calculations of such scattering of high energy electrons or protons have been made by Rose (22a), Rosen-

bluth (23), and by Saakyan (24). Parzen (25) has made some calculations for 100 Mev electrons on Pb, and Amaldi, Fidecaro & Mariani (26) for 300 Mev electrons on Li and C.

Radiation accompanying large angle scattering of electrons becomes somewhat important at very high energies, and it has been pointed out that  $\mu$  mesons of a few hundred Mev would be more suitable for probing the charge and current distributions in nuclei [Amaldi *et al.* (27)].

#### SCATTERING OF ELECTRONS AND POSITRONS BY ELECTRONS

The theory of electron-electron and positron-electron scattering has not been modified significantly since the calculations of Møller and of Bhabha (1). Some higher order corrections to electron-electron scattering have been considered by Takibaev (28).

The observation of the scattering of positrons and electrons from  $\text{Cu}^{64}$  in a cloud chamber filled with methane has been reported by Ritter *et al.* (29) to be in agreement with theory, but with insufficient statistics to check important details of the theory. Hoke (30) reports similar results in He. An experiment with radioactive sources in which the electrons are selected by magnetic analysis, using coincidence methods for identifying the scattering events, was carried out by Page (31). Ashkin (32) has made similar measurements with positrons. Another experiment with 15.7 Mev electrons from a betatron, by Scott, Hanson, & Lyman (33) uses the unique energy of the scattered electrons to distinguish this scattering from nuclear scattering. These experiments agree with the Møller theory within the experimental errors of about 5 per cent. Barber, Becker, & Chu (33a) using 6.1 Mev electrons observe a scattering 4 to 8 per cent less than expected. This might be explained by radiative losses. Howe & MacKenzie (34) have reported measurements on the ratio of electron-electron to positron-electron scattering of 1.3 Mev particles. They find a ratio of  $1.82 \pm .11$  which can be compared with a theoretical value of 1.83.

Electron-electron collisions with 200 Mev incident electrons in photographic emulsions were studied by Barkas *et al.* (35) who also found the energy and angular distribution of knock-on electrons in good agreement with theory. Their report, however, does not include knock-on electrons above 30 Mev. Fisher (36) has observed the knock-on electrons from 250 Mev electrons passing through a cloud chamber in a strong magnetic field. In addition to lower energy secondaries he has observed more than 80 events in which the secondary electron has more than 30 Mev. The number and energy of these electrons agree with the Møller theory better than the statistics warrant. Similar results with positrons are not as conclusive but do not disagree with the Bhabha relation.

#### MULTIPLE SCATTERING

Although practically any treatment which is adequate to explain the multiple scattering of charged particles is adequate for the discussion of



electrons, it is perhaps appropriate to mention some of the experiments with electrons since such scattering is often involved in the interpretation of other results. The most important contribution to the theory was that made by Moliere (37) who obtained a more accurate expression for the screening angle for the heavier elements. This eliminated a large part of the reported discrepancies between earlier experiments and theory [Ref. (1), p. 198] but more accurate and systematic measurements are necessary before the agreement is very significant.

Moliere also presented the scattering distributions in terms of functions useful for many applications. The detailed angular distributions of 15.7 Mev electrons scattered by thin Au foils were measured by Hanson, *et al.* (38), and show good agreement with Moliere's distributions for small angles. Spencer & Blanchard (38a) have used another method of calculation, avoiding the small angle approximation, which improves the agreement with theory at larger angles.

A simpler derivation of Moliere's theory, a discussion of the connection of this theory with the theory of Goudsmit and Saunderson (39), and a recalculation of the functions entering into this theory is given in a recent paper by Bethe (39a). Other discussions comparing various calculations are made by Scott (40) and by Wang & Guth (41).

The use of the multiple scattering of electrons in emulsions to determine the energy of an electron is common in many laboratories. The scattering constant of emulsion has been determined by use of electrons by Corson (42), Voyvodic & Pickup (43), and by Gottstein *et al.* (44). Voyvodic & Pickup and also Berger (45) discuss in considerable detail the various multiple scattering theories and their application to scattering in emulsions. In certain special cases, such as the effect of multiple scattering of electrons on the asymmetry in angular correlation measurements, the exact method of Goudsmit and Saunderson is also the simplest [Frankel (46)]. Other special cases were referred to earlier as corrections to nuclear scattering [Reich (9); Lipkin (10)].

#### IONIZATION LOSS

A number of recent experiments have done much to establish reliable ionization loss relations which cover the complete range of particle velocities. In this section we are concerned only with electrons or other particles whose velocities are appreciably greater than those of any atomic electrons in the medium, and in particular with the energy regions in which the effect of polarization of the medium is important. A complete discussion of the more general results is given by Bethe & Ashkin (3).

Although the processes involved in the ionization losses by electrons are the same as those for heavy particles, an important difference lies in the fact that an electron may in effect lose up to one-half of its energy in a single collision. Such large losses introduce a straggling of energy after



passing through matter which is relatively much greater than that for heavy particles. The range of an electron having a given energy is therefore far from unique even in materials of low atomic number.

In most experiments with electrons or other high energy particles ( $v \sim c$ ) the high-energy secondary electrons escape from the ionization chamber or other detecting device before their energy is dissipated. The energy loss detected in such devices is therefore not the average energy loss but that part associated with individual losses less than a certain value  $T$  determined by the absorption in the chamber. It will be useful to refer to the usual ionization loss equation in the form,

$$-\frac{dE}{dx} = \frac{2\pi ne^4}{mv^2} \left[ \log \frac{2mv^2T}{(1-\beta^2)(h\nu_m)^2} - \beta^2 \right] \quad 2.$$

where  $\nu_m$  is the mean absorption frequency of the medium. This relation is valid as long as the effect of polarization is negligible.

The mean excitation energy  $I = h\nu_m$  appearing in this relation has been determined with considerable precision for a number of materials by Bakker & Segrè (47) and by Mather & Segrè (48), from accurate measurements of the ranges of 300 Mev protons in the materials. It was pointed out by Bohr (49) that in conductors of low atomic number such as Be a large fraction of the electrons in the medium are essentially free and that the effective excitation potentials are expected to be considerably different from (somewhat surprisingly, higher than) those of the individual atoms. There are large variations in the measured values of  $I$  from the Bloch relation ( $I = kZ$ ) among the light elements. The value of  $I = 150$  ev for Al seems particularly well established. For the heavier elements it was found that  $I$  is given approximately by the relation  $I = 9.6 Z$ .

The effect of the polarization of the medium on the energy loss has been definitely established by experiment. The theory of this effect, first treated by Fermi (50), has been extended to describe more nearly the actual dielectric properties of materials. Detailed calculations for a number of the commonly used materials have been made by Wick (51), Halpern & Hall (52), and Sternheimer (53). Although the variation of the energy loss with the velocity of the incident particle depends upon the detailed frequencies assumed to describe the medium, all the calculations agree that the energy loss (associated with maximum energy transfers less than some definite value  $T$ ) for very high energies is given by the relation

$$-\frac{dE}{dx} = \frac{2\pi ne^4}{mv^2} \left[ \log \frac{2mv^2T}{(h\nu_p)^2} \right] \quad 3.$$

where  $\nu_p = (ne^2/\pi m)^{1/2}$  is the plasma frequency of the medium. The energy loss in this asymptotic region, where  $\nu_p/(1-\beta^2)^{1/2}$  is considerably above the  $K$  electron frequency, depends upon the properties of the medium only through the electron density  $n$ . A good qualitative discussion of the way this plasma frequency enters the theory has been given by Bohr (49).

The quantities necessary for determining the energy loss have recently been recalculated by Sternheimer (53). These are adjusted to agree with the experimental values of  $I$  at lower velocities and also to give the correct limiting value at high energies.<sup>2</sup>

The most probable energy loss depends upon the thickness  $t$  of the absorber, since higher energy secondaries are stopped in thicker absorbers. This energy loss as given by Landau (54) is

$$\Delta E_p = \xi t \left[ \log \frac{2mv^2 \xi t}{(1 - \beta^2)(h\nu_m)^2} - \beta^2 + 0.37 \right] \quad 4.$$

where  $\xi t = 2\pi n e^4 t / (mv^2)$  also represents an effective maximum energy transfer which contributes to the approximately Gaussian distribution, and the constant 0.37 represents the contribution of energy transfers greater than  $\xi t$ .

The widths of the straggling distributions at half maximum as calculated by Landau (on the assumption that the electrons in the medium are essentially free), is about  $4 \xi t$ . This width in most practical cases is about 20 per cent of the most probable energy loss.

The effect of polarization on the most probable energy loss is the same as before, and in the limit of extreme relativistic velocities depends only on the electron density in the medium. This asymptotic loss can be expressed by the simple relation

$$\Delta E_p = \xi t \left[ \log \frac{2mv^2 \xi t}{(h\nu_p)^2} + 0.37 \right] = \xi t \left[ \log \frac{t}{a_0} + 0.37 \right] \quad 5.$$

where  $a_0$  is the Bohr radius of hydrogen.<sup>3</sup>

Experiments with electrons from radioactive sources were made by Chen & Warshaw (55). They find the probable energy loss of 0.08 Mev to 1.03 Mev electrons in Al to agree with the Landau expression (equation 4 above). Similar but less extensive results were reported by Kageyama & Nishimura (56). In this low-energy region the effect of polarization is not important except for the conduction and loosely bound electrons. These are taken into account by using the experimental value of  $I$  measured for that material.

The widths of the observed straggling distributions for low-energy electrons were greater than those given by Landau as were the old measurements of White & Millington (57). These increased widths of the straggling

<sup>2</sup> It appears that the confusion about the constants in the energy loss formula mentioned by Sternheimer is of some importance in accurate calculations. It would seem advisable to use  $2mv^2$  in the argument of the logarithm, rather than  $2.72 mv^2$  as implied by Sternheimer's equation (11), since the experimental values of  $I$  were determined by using this expression [Sternheimer (53a)].

<sup>3</sup> Although the density effect as calculated by Sternheimer is the most useful one, since it is based on the experimental values of  $I$  at low energies, his equation (16) should be modified to agree with the above limit at extreme relativistic velocities. [Sternheimer (53a)].

distributions were considered by Blunck & Leisegang (58) who found that they could account for the classic distributions of White and Millington as well as other measurements by including the relatively large individual energy losses involved in the excitation of *K* and *L* electrons.

Energy loss measurements with 2 to 5 Mev electrons from a betatron were reported by Paul & Reich (59). These measurements were made with rather poor resolution and required considerable interpretation [Schultz (60)]. Their losses show a polarization effect in agreement with theory. They also tried to detect differences in stopping power associated with crystal structure but failed. Such effects are slightly larger for lower velocity incident particles and have been observed in precise measurements by Thompson (61) using 300 Mev protons.

The energy loss suffered by monoenergetic 15.7 Mev electrons from a betatron has been studied by Goldwasser, Mills & Hanson (62) who find the energy loss distributions in light elements in excellent agreement with those of Landau. The most probable energy losses in light elements are in good agreement with the asymptotic expression (equation 5 above). The observed energy loss in Au was somewhat less than that expected but the straggling distribution was accounted for by including the effects of the *K* and *L* electrons and radiation losses.

The effect of the radiative losses on the most probable loss is small. It accounts for an increase of less than 3 per cent even in the case of Au, where the average radiation loss is considerably greater than the ionization loss. The reason for this is that radiative losses consist of relatively large energy losses which do not contribute to the approximately Gaussian distribution. The effect on the energy distribution is considered by Shultz (60).

In many cases it will be of importance to correct for the increase in the path lengths of electrons in the medium that arise from multiple scattering. This effect in foils which are not too thick has been calculated by Yang (63).

The polarization effect in the region of transition from nonrelativistic to relativistic energies has also been investigated with cosmic ray particles. Bowen & Roser (64) have measured the energy loss distributions of selected cosmic ray  $\mu$  mesons in an anthracene crystal. They find the energy loss to be in agreement with the Landau expression, with the Halpern and Hall correction for polarization. This work represents a complete measurement of the variation of energy loss with energy, and the agreement with theory at both low and extreme relativistic velocities constitutes a welcome check on the calculations. These results are shown in Figure 3. Similar, though less detailed, results for sodium iodide crystals have been obtained by Hudson & Hofstadter (65). Other experiments have given information on the variation of the energy loss in gases and in emulsions. Ghosh, Jones & Wilson (66), using cloud chamber techniques, found the energy loss at high energies in oxygen to be about 30 per cent greater than that at the minimum.

Shapiro & Stiller (67) report an increase of 12 per cent in the grain density of electron and meson tracks in nuclear emulsion. Pickup & Voyvodic (68) report a 10 per cent increase.

Although such results did not arouse any immediate curiosity, it was pointed out by Messel & Ritson (69), and by Schoneberg (70) that, according

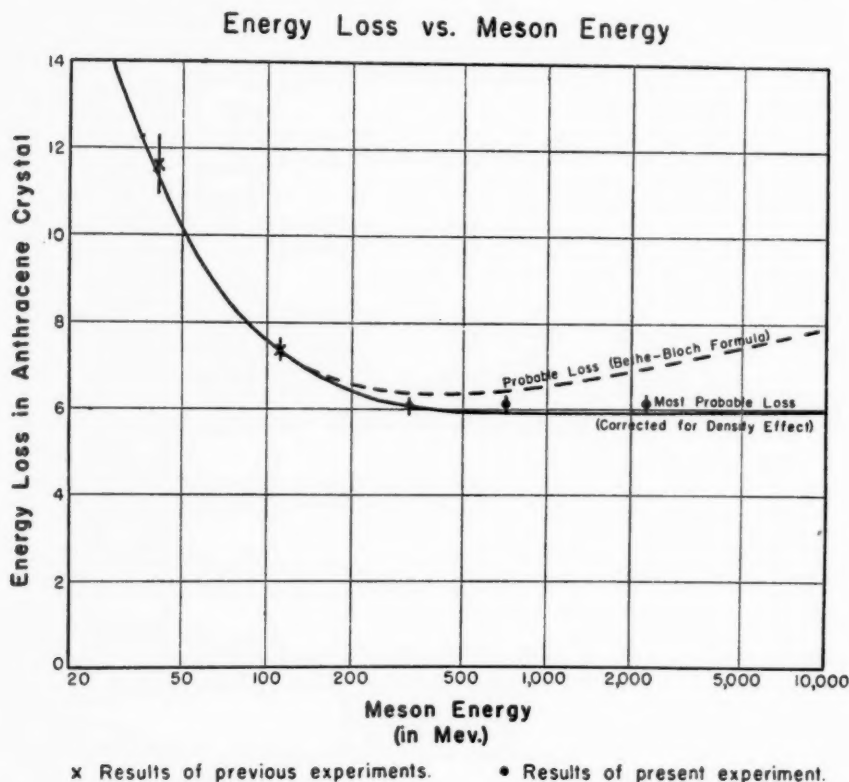


FIG. 3. Energy loss rate versus kinetic energy for  $\mu$  mesons in an anthracene crystal. From Bowen & Roser (64).

to the theory of Fermi (50), this increased energy loss should be carried away by Cerenkov radiation. From this point of view one might not expect an increase in the observable ionization above the minimum in oxygen. The large observed increase of 30 per cent indicates that most of the increased energy loss is absorbed locally.

Schoneberg & Huybrechts (71) have introduced a modified theory to account for this result. This theory leads to a distribution of the energy losses between ionization and Cerenkov radiation which is different from

that of the other theories. The principal result is that high energy Cerenkov radiation is suppressed.

Sternheimer (72) has considered the escape of Cerenkov radiation from AgBr grains in emulsion. He finds the energy escape to be very small when damping is introduced into the dispersion theory of the medium, which answers the question raised by Messel & Ritson (69) and by Schoneberg (70). In the region of visible radiation, the damping is negligible and the Cerenkov radiation is again given by the usual expression of Frank and Tamm. A similar calculation [Sternheimer (53a)] also accounts for the observed ionization in oxygen.

#### PAIR PRODUCTION

For  $\gamma$ -ray energies above a few Mev the major absorption process is that of pair creation. During the past few years the pair cross section has been the subject of extensive measurement with good precision in elements of widely differing atomic number and with widely differing  $\gamma$ -ray energies.

The theory of the pair process in the nuclear Coulomb field was originally developed by Bethe & Heitler (73) and is summarized in an excellent manner by Bethe & Ashkin (3). The original calculations were made using the Born approximation and are valid as long as  $(Z/137)(c/v) \ll 1$ . Here  $Z$  is the atomic number of the absorber and  $v$  is the velocity of the electron or of the positron produced. The Born approximation cross section for the creation of a pair in the Coulomb field of a bare nucleus is

$$\sigma_{pr} = \bar{\sigma} \left( \frac{28}{9} \log \frac{2h\nu}{mc^2} - \frac{218}{27} \right) \quad 6.$$

where  $\bar{\sigma} = (Z^2/137)(e^2/mc^2)^2 = 5.793 \times 10^{-28} Z^2 \text{ cm}^2$ . For lead  $\bar{\sigma} = 3.89$  barns.

The simple  $Z^2$  dependence of equation 6 is incorrect for three reasons: (a) the pairs may be created at a distance from the nucleus where the bare nuclear Coulomb field is modified by the screening effect of atomic electrons; (b) pairs may be created in the field of an atomic electron, a process which is difficult to distinguish experimentally from the nuclear field pairs; and (c) the Born approximation is invalid in the case of heavy elements or low electron or positron energy.

Screening by atomic electrons may be neglected if  $mc^2 \ll h\nu \ll (137 mc^2/Z^{1/3})$ . In heavy elements this condition is never well satisfied; for example, in Pb the upper limit is 16 Mev. Therefore, in heavy elements and at high energies, screening must be considered. If  $h\nu \gtrsim (137 mc^2/Z^{1/3})$ , an appreciable fraction of the pairs is created at distances from the nucleus where screening is important. At sufficiently high energies the cross section becomes independent of energy. For this case the screening is "complete" and the pair cross section can be integrated analytically. The result, first calculated by Bethe and Heitler, is

$$\sigma_{pr} = \bar{\sigma} \left[ \frac{28}{9} \log \frac{183}{Z^{1/3}} - \frac{2}{27} \right] \quad 7.$$

At intermediate energies numerical integration must be resorted to when shielding is taken into account. Bethe & Heitler (73), and Bethe & Ashkin (3), give data for making such calculations. For the limit of low energies where equation 6 is also invalid, Hough (74) has published calculations. Bethe (see 75) has pointed out a convenient way to find the screened cross section in a given element at various energies using the data from some other element over a range of energies.

The cross sections given by equations 6 and 7 above represent the nuclear field process only, and for any comparison with experiment the electronic field process must also be included. For  $\gamma$ -ray energies above 20 Mev screening becomes important, and Wheeler & Lamb (76) have made the appropriate calculation. For the screened case the ratio of the electronic to the nuclear field cross section can be expressed [Bethe and Ashkin (3)] as

$$\sigma_{el}/\sigma_{nuc} = x/Z \quad 8.$$

where  $x$  is a quantity slightly greater than unity, the particular value depending on  $Z$ ; it varies from 1.40 for  $Z=1$  to 1.14 for  $Z=92$ , when the screening is complete.

For  $\gamma$ -ray energies less than 20 Mev, unscreened cross sections can be used and calculations of Borsellino (77) have usually been used in interpreting experiments in this energy range. The electronic field cross section can be expressed as in equation 8, where the value of  $x$  decreases rapidly as the  $\gamma$ -ray energy decreases, falling to zero at the threshold energy of  $4 mc^2$ . Calculations of the electron field pair cross section have also been made by several other authors (78).

To include the effect of pairs created in the atomic electron field, then, the factor  $Z^2$  in equations 6 and 7 must be replaced by  $Z(Z+x)$ .

Deviations from the Born approximation cross section at low energy were evident in the early calculations of Jaeger & Hulme (79) and of Jaeger (80). They used exact Dirac wave functions, and calculated cross sections for Pb about 25 per cent higher than the Born cross sections at a  $\gamma$ -ray energy of  $5 mc^2$ , and about 100 per cent higher at  $3 mc^2$ . They also suggest a  $Z$  dependence of the form  $aZ^2 + bZ^4$  at these low energies.

Recently Maximon & Bethe (81) have published an exact calculation of the differential pair cross section in the limit of high relativistic energies, neglecting screening, and Davies & Bethe (82) have performed the integration over all angles to get the total cross section. The result is to correct the Born cross section downward, so that the exact bare nuclear field pair cross section for lead is given by

$$\sigma_{pr} = \bar{\sigma} \left[ \frac{28}{9} \log \frac{2h\nu}{mc^2} - \frac{218}{27} - \frac{28}{9} (0.33) \right] \quad 9.$$

where the  $(28/9)(0.33)$  term is the correction. This produces an 11.8 per cent reduction in the cross section in Pb at 88 Mev and 10.0 per cent at 280



Mev. This high-energy calculation is invalid for  $\gamma$ -ray energies below about 40 Mev. The same correction may be applied to all Born approximation calculations, screening included, of the nuclear pair cross section, the correction term being approximately  $(28/9)1.21(Z/137)^2$  when the cross sections are written in the form of equations 6 and 7.

We expect the general features of the pair process to be represented by the Born approximation cross section, with actual cross sections in heavy elements becoming appreciably larger than the Born value at low  $\gamma$ -ray energies and somewhat smaller than the Born value at higher energies. In each case the deviations are expected to have a strong  $Z$ -dependence.

The recent measurements with uncertainties generally less than 2 per cent, covering energies from 1.3 to 300 Mev and covering elements from Li to U, show remarkable agreement with the calculations, provided electron field pairs, screening and the deviations from the Born approximation are taken into consideration. The measurements are to some extent indirect, but they are probably nonetheless reliable.

The direct cross section measurement of any  $\gamma$ -ray process, involving counting the number of events for a given  $\gamma$ -ray flux through a given absorber, is difficult because of the uncertainties in measuring the  $\gamma$ -ray flux. No such measurement has been attempted in the case of pair production. Relative pair cross section measurements in different elements at a given  $\gamma$ -ray energy is reasonably straightforward and has been the subject of a number of experiments. In this case, only relative  $\gamma$ -ray fluxes are required, so that absolute calibration of the monitor is unnecessary. In these measurements the Born approximation is assumed to give the correct result for light elements, and the relative cross sections then give deviations from the Born values directly.

Measurement of the attenuation coefficient for a beam of  $\gamma$ -rays passing through an absorber is also relatively straightforward. In this case, the total absorption and scattering cross section is measured and the pair production part is sorted out in a somewhat indirect manner. For many cases of interest, however, the attenuation is predominantly by the pair process so that the competing cross sections need not be known with great accuracy. The principal competing process is the Compton effect and the cross section for this is believed to be accurately given by the Klein-Nishina equation. The chief danger lies in the possibility that a photon will be Compton scattered and still lie within the angular and energy discrimination of the detector. This effect becomes especially important when the  $\gamma$ -rays constitute a *bremsstrahlung* spectrum. The use of high resolution, energy-sensitive detectors or rigorous collimation serve to reduce this effect to negligible proportions. At low  $\gamma$ -ray energies the ordinary atomic photoeffect must be considered, but again this can be done with sufficient precision. At  $\gamma$ -ray energies around 20 Mev the nuclear photoeffect displays a broad resonance and contributes a minor percentage, the exact figure not being actually



known, to the total cross section. This contribution is relatively larger in the lighter elements.

In comparing measured attenuation cross sections with calculated values, the procedure is to calculate a cross section using the Born approximation including screening and electron field pairs, add the Klein-Nishina Compton cross section, and also the atomic and nuclear photoeffect cross sections if they are required. The difference between this calculated cross section and the measured one is attributed to failure of the Born calculation for nuclear field pairs. When this comparison is made for light elements the Born cross section is found to be correct to within the uncertainties of the measurements so that the procedure adopted in the relative cross section measurements is justified. In discussing attenuation measurements in this paper we arrive at "measured" nuclear pair cross sections by the subtraction process outlined above.

Measurements of the relative cross section type near the pair threshold have been made by Hahn, Baldinger & Huber (83) and later by Dayton (84), using radioactive  $\gamma$ -ray sources. Both experiments show close agreement with the calculations of Jaeger & Hulme (79, 80) for the  $Z$ -dependence of the nuclear pair cross section.

There is also evidence from the work of Cleland, Townsend & Hughes (85) on the internal pair conversion of the nuclear  $\gamma$ -rays that the ordinary pair cross section deviates from the simple  $Z^2$  dependence in the same general way as indicated in the experiments of Hahn *et al.* (83) and of Dayton (84).

Adams (86) has covered the range from 10 to 20 Mev with attenuation measurements in Al, Fe, Cu and Pb using a betatron *bremssstrahlung* spectrum and threshold detectors. The measured attenuations are in good agreement with calculated cross sections based on the unscreened Born approximation in Al, Fe and Cu. In Pb, Adams finds the "measured" nuclear pair cross section appreciably lower than the Born value and he also finds the deviation to be energy dependent. The energy dependence is not real, however, since it arises from his failure to take account of screening in calculating his theoretical cross sections. In Pb at 19 Mev, screening reduces the nuclear pair cross section by 5 or 6 per cent, which is about the magnitude of the energy-dependent part of his deviation. Eliminating this, his data give a downward deviation from the Born cross section of about 8 or 9 per cent.

Berman (87), in an abstract, has reported a measurement of the same type as Adams', covering 19 elements at 19.5 Mev. His results indicate a ratio of "measured" to Born cross section varying from 0.95 in Sn down to 0.87 in Pb.

Attenuation measurements have been made in the 5 to 20 Mev range by Rosenblum, Shrader & Warner (88) using a *bremssstrahlung* source and a  $180^\circ$  pair spectrometer as detector. In this measurement a narrow energy band well below the maximum betatron energy was selected by means of

the high-resolution energy-sensitive detector. Detection of degraded radiation is avoided by using rigid collimation. Measurements are made at 5.3, 10.3, and 17.6 Mev using Cu, Sn, Pb, and U absorbers. The data show the interesting property that the deviation from the Born cross section is upward at 5.3 Mev, in agreement with the measurements of Hahn *et al.* (83) and of Dayton (84), while it is downward at higher energy.

Walker (89, 90) has made extensive measurements of the attenuation coefficient and also of relative pair cross sections directly using the 17.6 Mev  $\gamma$ -ray from the  $\text{Li}^7(p, \gamma)\text{Be}^8$  reaction. In each case he used a  $180^\circ$  pair spectrometer as the energy-sensitive detector. The attenuation measurements show the ratio of "measured" nuclear pair cross section to the Born value in light elements to be about unity, falling to 0.90 in Pb.

Walker measures the relative pair cross sections in several elements between Li and Pb, using the same 17.6 Mev  $\gamma$ -ray and the spectrometer detector. In comparing measured and calculated values he takes account of the screening correction to the bare nucleus Born value, and of the electron field pair cross section by writing

$$\sigma_{\text{Born}} \sim Z(Z+x)[1-S(Z)] \quad 10.$$

where  $S(Z)$  is the screening correction. At 17.6 Mev,  $S(Z)$  varies from 0.01 for Li to 0.05 for Pb;  $x$  has an interpolated value of 0.68 from Borsellino's unshielded electron field calculation. Walker finds a measured value for  $x=0.8 \pm 0.3$  by plotting, for the light elements where the Born nuclear field cross section is assumed correct,  $\sigma_{\text{meas}}/Z[1-S(Z)]$  versus  $Z$ . His relative pair cross sections show a bigger deviation from the Born value than do the attenuation cross sections, the ratio of measured to Born value dropping to 0.89 in Sn and 0.85 in Pb.

It should be noted that Walker's measurements refer not to the total cross sections but only to that portion of it in which the members of the pair receive energy in the range from 0.25 to 0.75 the total available energy. Since the correction to the Born approximation value is probably different for small positron energies compared to small electron energies this may make some small difference in the total cross sections.

Lawson (91) was the first to make extensive attenuation measurements of the type discussed here. He measured attenuation coefficients in several elements from Be to U, using the upper end of a *bremsstrahlung* spectrum with a pair spectrometer as detector. In finding calculated values to compare with his measured attenuation coefficients, Lawson makes a rough check on the Klein-Nishina Compton cross section, and shows that it is correct within the uncertainty of the measurement, which is about 15 per cent.

Lawson's results are closely similar to Walker's, the ratio of "measured" to calculated cross sections at 88 Mev falling to 0.88 in U. He finds a ratio of 1.13 in Be, but this is unconfirmed by any other experiment and may result from impurities.

The highest energy at which pair cross sections have been determined is

280 Mev in the work of DeWire, Ashkin & Beach (75). These measurements were made using a *bremstrahlung* source and a pair spectrometer detector. As in the work of Lawson, attenuation coefficients were measured for several different absorbers. The results agree closely with Lawson's

The final measurement of the pair process to be discussed here is that of Emigh (92), who used a cloud chamber to measure the relative number of pairs produced in two foils through which a *bremstrahlung*  $\gamma$ -ray beam passes. Direct cross section ratios for Au to Al, Ag to Al, Au to Ag, and Th to Al are measured for the energy range from 50 to 300 Mev. Deflection in a magnetic field serves to determine the energy of the pair members. In all, some 46,000 pairs have been measured. Within the uncertainties of the experiment (about 3 per cent) the ratio of measured to calculated relative (to Al) cross sections are independent of energy. The ratios of measured to calculated cross section show the same behavior as in the other high-energy experiments.

The combined results of all the pair cross section experiments discussed above are shown in Table I.

The data for Pb are plotted in Figure 4, together with the calculated

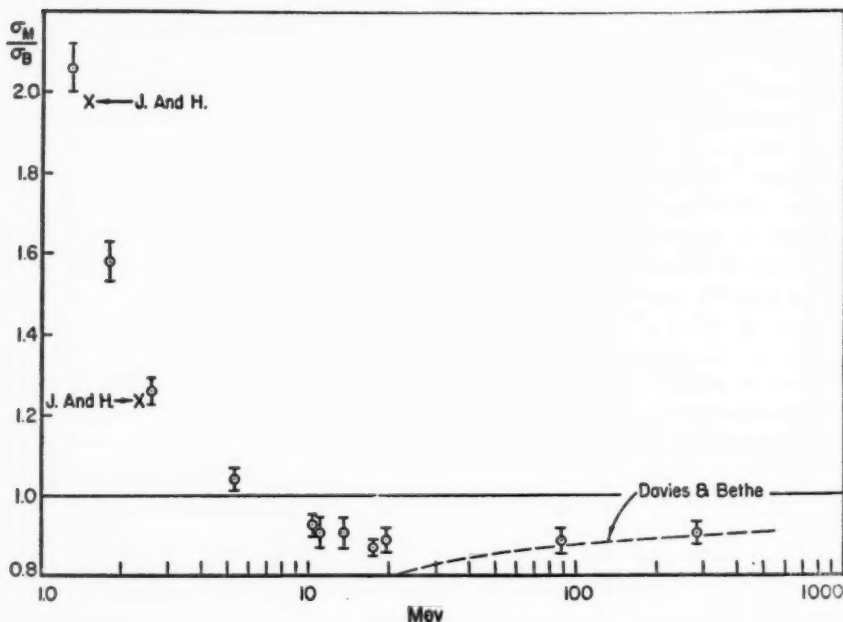


FIG. 4. Ratio of "measured" to Born approximation pair cross section (bare nucleus) in lead. Calculated points of Jaeger & Hulme (79, 80) and calculated curve of Davies & Bethe (82) are indicated.

TABLE I

## RATIO OF MEASURED TO BORN PAIR CROSS SECTIONS

( $\sigma_{\text{meas}}/\sigma_{\text{Born}}$ ) for nuclear field pairs from attenuation cross sections and from relative pair cross sections. Born approximation cross sections are assumed correct for light elements. All discrepancies between measured and calculated cross sections are attributed to failure of the Born calculation for the nuclear pair process. Uncertainties are generally less than 2 per cent.

	Mev											50- 300
	1.3	1.8	2.6	5.3	10.3	11.0	13.7	17.6	19.1	88	280	
Li								1.00				
Be			1.08							1.13	1.03	
C			.93					.99				
								1.02				
Al	1.00		1.01			.99	1.01	.99	1.02	1.03	1.01	
			.94					1.01				
Fe	1.04	1.06	1.02			.99	1.01		1.02			
Cu	1.11	.98	1.03	.97	1.01	1.00	1.03	1.04	1.02	1.03	.99	
			1.01					1.01				
								.94				
Ag												.97
Sn	1.49	1.28	1.08	1.06	1.00			.98	.95	.96	.97	
	1.47		1.18					.96				
								.89				
Au												.92
Pb	2.08	1.58	1.33	1.04	.93	.91	.91	.90	.87	.89	.91	
	2.04		1.23					.87				
								.85				
Th												.88
U		1.64		1.06	.92			.87		.88	.89	

points of Jaeger and Hulme and with the corrected Born curve of Davies and Bethe. It is evident that the Born approximation cross section is correct at an energy somewhere between 5 and 10 Mev. Furthermore, examination of the data in Table I shows that the Born value is correct for all atomic numbers at this energy.

The  $Z$ -dependence of the deviation from the Born result is shown in Figure 5 where ( $\sigma_{\text{meas}}/\sigma_{\text{Born}}$ ), averaged for all energies of 17.6 Mev and above, is plotted against  $Z^2$ . The deviation of the "measured" cross section from the Born value is well represented by  $Z^2/625$  per cent of the Born value.

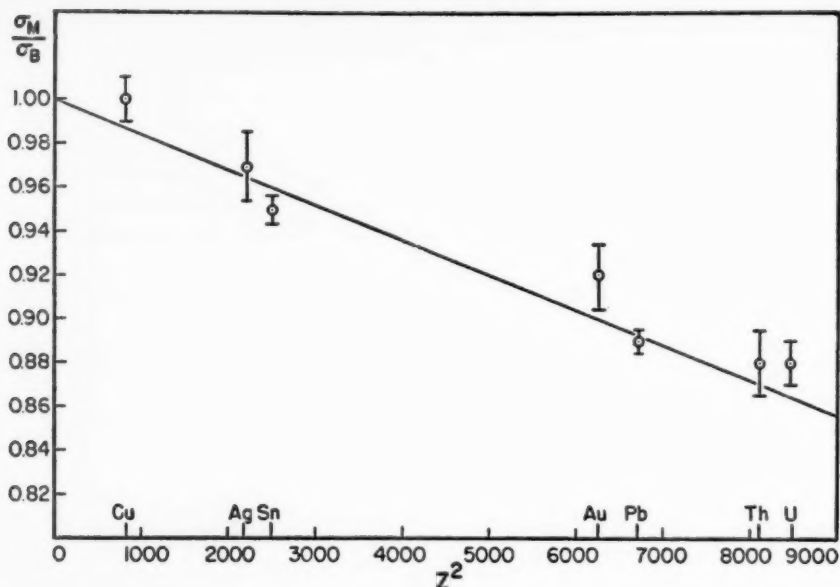


FIG. 5. Ratio of "measured" to Born approximation pair cross section (bare nucleus) as function of  $Z^2$ . All data for energies of 17.6 Mev and above have been averaged together. Straight line represents deviation of  $Z^2/625$  per cent.

### Bremsstrahlung

The *bremsstrahlung* process in which a high velocity charged particle radiates a photon when it is accelerated in the Coulomb field of a nucleus (or of an electron) is closely related to the pair production process, the same type of cross section calculation being applicable in each case. Bethe & Heitler (73) calculated the nuclear field *bremsstrahlung* cross section for relativistic electrons in the same paper in which the pair cross section was calculated. The calculations are subject to the same Born approximation discussed in the pair case and to the same atomic electron screening considerations. As in the case of pair production there are two limiting cross sections, one for the bare nucleus and one for the completely screened nucleus. These are

$$\sigma(E_0, \nu) d\nu = \bar{\sigma}_4 \left[ 1 + \left( \frac{E}{E_0} \right)^2 - \frac{2}{3} \frac{E}{E_0} \right] \left( \log \frac{2E_0 E}{mc^2 h\nu} - \frac{1}{2} \right) \frac{d\nu}{\nu} \quad 11.$$

for the bare nucleus, and

$$\sigma(E_0, \nu) d\nu = \bar{\sigma}_4 \left\{ \left[ 1 + \left( \frac{E}{E_0} \right)^2 - \frac{2}{3} \frac{E}{E_0} \right] \log \frac{183}{Z^{1/3}} + \frac{1}{9} \frac{E}{E_0} \right\} \frac{d\nu}{\nu} \quad 12.$$

for the completely screened case. In these equations  $\sigma(E_0, \nu) d\nu$  is the cross section for the production of a photon in the frequency interval  $d\nu$  at fre-

quency  $\nu$  by an electron of total energy  $E_0$ .  $E$  is the electron's total energy after radiating.  $\bar{\sigma} = (Z^2/137)(e^2/mc^2)^2$ , as in the pair discussion. For intermediate cases numerical integration is required to include the screening effects, and the results are given in convenient form by Bethe & Ashkin (3). The effect of screening is to reduce the cross section for the production of low-energy quanta compared to high-energy quanta. It is evident from equation (12) that in the completely screened case the cross section is a function only of  $E/E_0$ , i.e., the probability of a given fractional energy loss is independent of the incident energy.

The cross sections in equations 11 and 12 diverge as the photon energy approaches zero. However, if we consider the quantity,  $h\nu\sigma(E_0, \nu)d\nu$ , which represents the energy radiated in the interval  $d\nu$ , the result is finite and it is

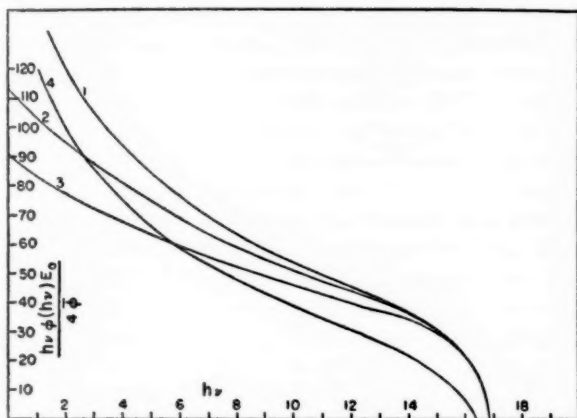


FIG. 6. Bremsstrahlung intensity distribution as a function of photon energy from 16.93 Mev electrons. Curve 1: unscreened nucleus; curve 2: Be; curve 3: Au; curve 4: electron-electron collisions. From Lanzl & Hanson (93).

convenient to plot the cross section in this form. Several examples are shown in Figure 6, which is taken from a paper by Lanzl & Hanson (93). These curves show the more or less flat energy distribution characteristic of *bremsstrahlung*. As the primary electron energy increases, the flatness becomes more pronounced. When screening is neglected the energy distribution is independent of  $Z$ .

Equations 11 and 12 represent only radiation in the nuclear field and, as in the pair production case, corrections must be added for processes in the Coulomb field of the atomic electrons. This correction can be made in the same way as in the pair case by replacing  $Z^2$  in equations 11 and 12 by  $Z(Z+x)$  where  $x=1$  if  $mc^2 \ll E_0 \ll 137mc^2Z^{-1/3}$ . If  $E_0 \sim mc^2$ ,  $x$  is less than unity, whereas for high energy where screening is important  $x$  is slightly greater than unity, as in the pair case.

The Bethe-Heitler calculations are based on the Born approximation and so have been considered subject to correction in heavy elements. Bess (94) has made a calculation which is independent of the Born approximation and which shows a cross section greater than the Born value. However, Maximon and Bethe (81) point out that Bess' theory is in error, and that in the limit of high energy the *bremstrahlung* is reduced by the same amount as in the pair production case. However, it now appears (95a) that the Born approximation is correct in the limit of complete screening. At lower energies the Born cross section is subject to a downward correction, the magnitude of which is not now available. At the upper end of the radiated x-ray spectrum the Born approximation calculation leads to a cross section which goes to zero. Heitler (2) has shown that an exact calculation should lead to a finite cross section at the upper limit.

For relativistic electron energies the *bremstrahlung* radiation is predominantly in the forward direction, the average angle of emission (relative to the primary electron direction) being about  $mc^2/E_0$ , independent of the photon energy. The explicit angular distribution for small angles, neglecting screening, has been calculated by Sommerfeld (95) for the case where both  $E$  and  $E_0$  are large compared with  $mc^2$ . He finds a differential cross section per unit solid angle at angle  $\theta$  which depends both on  $\theta$  and on the energy of the radiated photon, so that the energy distribution of the radiation depends somewhat on the angle of emission. Hough (96) has also calculated the angular distribution for high energies and large angles (see 97a), with results somewhat different from Sommerfeld's. Hough gives curves for the angular distribution. Stearns (97) has calculated the mean square angle of emission for the screened case, and the effect of screening on the angular distribution has been calculated by Schiff (98). Borsellino (98a) has calculated the divergence angle of pairs produced by photons, taking screening into account.

Any observed x-ray distributions are modified by the multiple scattering of the electrons in the target prior to radiation. The distributions are further modified in the case of high-energy circular accelerators because the electrons may traverse the target several times before radiating. Schiff (98) has calculated the angular distribution taking the multiple scattering of the electrons into account and using the Williams (99) scattering theory. Lawson (100) has made a somewhat similar calculation using the Rossi-Greisen (101) scattering theory. The general effect of the electron scattering is to widen the distribution by an amount depending on the thickness of the target, and to make the energy distribution of the radiation independent of angle.

There are two general methods by which the *bremstrahlung* process can be studied experimentally: (a) by measuring the energy of the electrons before and after passing through a given target material; and (b) by measurements on the radiation itself. In the first method the energy loss by *bremstrahlung* is indistinguishable from energy loss by other processes, so the conclusions



concerning *bremsstrahlung* are somewhat indirect. The recent experiments mentioned here are of the second type. There are several different measurements which can be made: (a) the total cross section can be investigated; (b) the  $Z$ -dependence of the cross section can be determined; (c) the energy distribution of the radiation can be measured; and (d) the angular distribution of the radiation can be measured. Recent experiments have dealt with all these aspects of the problem.

Lanzl & Hanson (93) have measured the  $Z$ -dependence of the cross section for the production of *bremsstrahlung* above 10.9 Mev by 17 Mev electrons, using Cu threshold detectors. As in the measurements of Walker (90) on pair production, the effectiveness of atomic electrons for producing *bremsstrahlung* can be determined by measuring relative cross sections in a number of light elements. The value of  $x$  so determined is  $0.75 \pm .05$ . Using this number for the atomic electrons and using calculated screening corrections, the relative *bremsstrahlung* cross sections in the nuclear field are "measured" in the experiment. The results show the simple  $Z^2$  dependence from Be to Au of the Born approximation calculation, to within the experimental uncertainty of 1 per cent. It should be noted that Lanzl, Laughlin & Skaggs (102) previously reported an 8 per cent discrepancy between measured and calculated ratio of cross sections for Ta and Cu. Lanzl & Hanson (93) point out that proper treatment of the data removes this discrepancy. In the same experiments the relative cross sections for the total radiation are measured with ionization chambers. The relative cross section for Au is found to be slightly smaller compared to light elements than is indicated by a  $Z^2$  dependence. The small difference may represent incorrect screening or atomic electron field corrections. The measured absolute cross section agrees with the calculated value to within the experimental uncertainty of 10 per cent. Lanzl & Hanson (93) have also measured the angular distribution of the radiation produced by 17 Mev electrons. X-ray film, small ionization chambers, and wide angle threshold detectors were used as *bremsstrahlung* detecting devices. The results are in generally good agreement with Schiff's (98) and Lawson's (100) calculations, although the measured distributions are somewhat narrower than the calculated ones. When the Moliere (37, 39) multiple scattering theory is used, which gives a somewhat smaller multiple scattering distribution than those used by Schiff and Lawson, the agreement between measured and calculated distributions is excellent.

The energy distribution of the *bremsstrahlung* from 19.5 Mev electrons has been measured by Koch & Carter (103) through the cloud chamber observation of positron-electron pairs produced by the radiation from a 0.005 inch Pt betatron target. The observed number of pairs with total energy in a given energy interval is divided by the Born approximation pair cross section to find the corresponding number of photons in the same interval. The resulting spectrum is in reasonably good agreement with the Bethe-Heitler Born approximation spectrum, although Koch and Carter consider

that the measurements show relatively too many quanta with energies from 8 to 12 Mev.

The *bremsstrahlung* spectrum produced by 322 Mev electrons striking a 0.020 inch Pt target has been determined by Powell, Hartsough & Hill (104) using a cloud chamber. The measured energy spectrum of pairs formed in a 0.001 inch Pb radiator was converted into the *bremsstrahlung* spectrum with the aid of the Bethe-Heitler pair cross section. The resulting spectrum agrees with the Born approximation calculated spectrum within the statistical uncertainty of the measurement (some 200 pairs in each of 15 energy intervals).

Stokes (105) has made similar measurements on *bremsstrahlung* produced by 65 Mev electrons, with results that also agree with the Born approximation spectrum within the uncertainties of the measurement.

DeWire & Beach (106) have determined the *bremsstrahlung* spectrum produced by 312 Mev electrons striking a 0.0005 inch W target using a magnetic pair spectrometer. The spectrum, derived in the same way as that of Powell *et al.* (104), is in excellent agreement with the calculated spectrum. Curtis (107) and Fisher (36) have measured the radiation loss by observing the energy loss of the incident electron in passing through a small piece of high *Z* material in a cloud chamber. Curtis' measurements with 60 Mev electrons on Pb were not sufficiently accurate to be of more than qualitative value. Fisher has measured the losses of 250 Mev electrons and positrons in Au and has obtained reliable values of the cross section for radiative collisions in which the particles lose more than 2/3 of their initial energy. A preliminary value averaged over both positrons and electrons is about  $8 \pm 2$  per cent below that calculated according to the Born approximation.

It is interesting to note that DeWire and Beach's absolute *bremsstrahlung* intensity is only about 6 times as great with a 40 mil target as with a 0.5 mil target. Presumably the electrons traverse the target many times in the case of the thin target.

Lawson (108) has shown that the absolute radiation intensity in the forward direction is given by a simple relation for electrons above 5 Mev striking a thin target.

#### SUMMARY

As far as electron interactions are concerned, there is generally good agreement between theory and experiment, although further information is desirable on a number of points. These points include: (a) more accurate measurements of large angle electron and positron scattering at energies of a few Mev by heavy nuclei; (b) more complete multiple scattering measurements in foils of different atomic number and of different thicknesses; (c) further theoretical treatment of multiple scattering in solid materials of low atomic number; (d) measurements of the most probable energy loss in a number of materials as a function of electron energy in the transition

region; and (e) quantitative measurements of the Cerenkov radiation associated with energy loss in various solids and gases.

As far as  $\gamma$ -ray interactions are concerned, the pair cross-section measurements are in excellent agreement with calculated values. Other features of the process, not discussed in this paper, are also in good agreement, so that the pair process is now well understood. The measurements on the *bremsstrahlung* process, on the other hand, are much less extensive than in the pair case. The adequacy of the existing theory cannot be fully established until further measurements on all aspects of the process are available. Detailed features, such as the polarization [May & Wick (109); Gluckstern, Hull & Breit (110)] of the radiation, have yet to be measured.

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# NEUTRON OPTICS<sup>1</sup>

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With the advent of chain-reacting piles and their copious fluxes of slow neutrons, a new field of research came into being, the field of neutron optics, with applications ranging from the properties of subnuclear particles to long range order in solids. The high intensity, well-collimated beams of thermal neutrons from piles make it possible to demonstrate and utilize such well-known optical properties as diffraction, refraction, reflection, and polarization. Although the applications of these phenomena are widespread, they have as a unifying factor the dependence on the interference effects of slow neutrons. After a brief consideration of the underlying principles of neutron optics, we shall review the recent progress in this field. The task of the reviewer is simplified by the relatively small number of papers published to date, a situation undoubtedly related as much to the scarcity of available research piles as to the novelty of the techniques.

## NEUTRON-OPTICAL PRINCIPLES

In many respects the behavior of slow neutrons, for which the wave characteristics predominate over those of particles, is closely analogous to that of light or x-rays. The neutrons present in highest intensity in the pile are those in thermal equilibrium with the graphite moderator near room temperature (1, 2), and, as their wavelength is about one Ångström, the analogy with x-ray phenomena, studied with similar wavelengths, is particularly close. There are distinct differences between neutron and electromagnetic optics, however, differences that are essential to the most valuable applications of the new field. The two most important of these are the more numerous sources of incoherence and the magnetic interaction present in neutron scattering. The incoherent scattering that arises from "spin-flipping," for instance, is a powerful tool for investigation of the spin-dependence of nuclear forces, while magnetic scattering renders such structure properties as ferromagnetism, antiferromagnetism, and paramagnetism capable of direct study.

The principles of neutron optics can often be expressed most simply in terms of the analogy with electromagnetic waves. For example, the correction for temperature diffuse scattering in neutron diffraction can be taken over directly from x-ray theory [the Debye-Waller factor (3)]. Also, given the index of refraction, such phenomena as total reflection and depth of penetration follow the same equations for neutrons as for light or x-rays. The derivation of the fundamental parameters, however, such as the index of refraction or the incoherent scattering amplitude, is usually simpler if carried

<sup>1</sup> The survey of the literature pertaining to this review was concluded in February, 1953.



out directly for neutrons, with no regard to the electromagnetic analogy. Many of the fundamental relationships of neutron optics were developed in a series of papers of Halpern and co-workers (4 to 7), published several years before pile fluxes were available. These papers, primarily motivated by the magnetic effects in neutron scattering, constituted a review of the theory of coherence effects, crystal diffraction polarization, and refraction, and at the same time served as a preview of most of the experimental work performed since their publication. References to other theoretical treatments of coherent and incoherent effects in neutron scattering may be found in the review by Lax (8).

The question of coherence and incoherence introduces little difficulty in the optics of electromagnetic waves. For example, in calculation of the intensity in crystal diffraction the departure of the atoms from their average positions causes a decrease in the intensity coherently scattered into the Bragg peaks and the appearance of a diffuse incoherent background (3). This same incoherence occurs for neutron scattering (8), and, in addition, there is possible incoherence that occurs even for scattering from a single nucleus. This latter incoherence, defined as the incapability of interference for the scattered wave, is related to the possibility (for an initial non-zero spin) of change of the nuclear spin with simultaneous "flip" of the neutron spin (4).

The various types of incoherence in neutron scattering are given by the appropriate scattering amplitudes for each process, representing the distance the neutron wave is shifted by the scattering nucleus. The differential scattering cross section is given by the square of the amplitude,  $a$ , and the total scattering cross section by  $4\pi a^2$  if the scattering is isotropic. For nuclear scattering of neutrons by independent bound nuclei (a convenient fiction) the angular distribution is isotropic, but magnetic scattering, being a dipole-dipole interaction, has a somewhat involved distribution.

For any nucleus of nonzero spin, there will be two amplitudes,  $a_+$  and  $a_-$ , corresponding to the two possible spins of the compound nucleus,  $i \pm \frac{1}{2}$ , formed by combination of the neutron with the target nucleus of spin  $i$  (4). The compound states are not equally probable but are weighted in the ratio  $i+1$  to  $i$ , hence the coherent amplitude, which is the weighted mean, is just

$$a_{\text{coh}} = \frac{i+1}{2i+1} a_+ + \frac{i}{2i+1} a_-, \quad 1.$$

and the coherent cross section, neglecting interference with other nuclei, will be given by  $4\pi a_{\text{coh}}^2$ . As the total intensity is the sum of the contributions of the spin states, the total amplitude is given by,

$$a_t = \left( \frac{i+1}{2i+1} a_+^2 + \frac{i}{2i+1} a_-^2 \right)^{1/2}. \quad 2.$$

Finally, the incoherent amplitude is obtained from the difference between the total intensity and the coherent intensity ( $a_{\text{inc}}^2 = a_t^2 - a_{\text{coh}}^2$ ),

$$a_{\text{ine}} = \frac{\sqrt{i(i+1)}}{2i+1} (a_+ - a_-). \quad 3.$$

If there are no resonances near thermal,  $a_+$  and  $a_-$  will be about the same and equal to the nuclear radius ( $1.5 \times 10^{-13} A^{\frac{1}{3}}$  cm., where  $A$  is the atomic weight); as a result the spin-dependent incoherent scattering will be small. Near a resonance, however, the scattering amplitude of a nucleus with non-zero spin will change rapidly for one of the spin states only (for the resonance has a definite spin  $i + \frac{1}{2}$  or  $i - \frac{1}{2}$ , and marked spin-dependent incoherence will result (9). If the resonance is at an energy slightly above thermal, one of the amplitudes may be negative and there is a possibility that  $a_{\text{coh}}$  may by chance be zero, a situation that is almost attained for vanadium, Table I. For hydrogen, the amplitude is negative because the negative amplitude of the singlet state ( $i - \frac{1}{2} = 0$ ) is so large that it outbalances the triplet amplitude ( $i + \frac{1}{2} = 1$ ) in spite of the 3:1 weighting.

When more than one nucleus is considered, incoherence may result even for a single element if it has isotopes of different amplitudes, for they are, of course, distributed at random. The equations for this isotopic incoherence are just the same as those given for spin incoherence with the isotopic abundances substituted for the spin weighting factors, and we shall not quote them. In practice it is usually possible to distinguish isotopic from spin-dependent scattering by the use of separated isotopes. Correction for the reduction in coherent scattering caused by lattice vibrations that occurs in neutron diffraction is made by means of the Debye-Waller factor just as done with x-rays (10); for mirror reflection, where only forward scattering occurs, the Debye-Waller factor is unity.

The coherent scattering of neutrons in crystalline material produces Bragg reflections at angles satisfying the relation

$$n\lambda = 2d \sin \theta, \quad 4.$$

where  $\theta$  is the angle between the neutron direction and the reflecting crystal plane,  $d$  is the interplanar spacing, and  $n$  the order of the reflection (3). The pattern of the various Bragg reflections will have a characteristic appearance depending on the nature of the crystal and the geometrical arrangement of sample and detector (11). In strict analogy with x-rays, Laue patterns may be obtained by diffracting polychromatic neutrons in a single crystal, although the method is extremely tedious (12). In the rotation method, monochromatic neutrons are diffracted from a single crystal as the angular position of the crystal is varied (13), and in the Debye-Scherrer or powder method (14), monochromatic neutrons are incident on a polycrystalline sample and diffract into cones around the direct beam. While all of these conventional x-ray techniques have been duplicated for neutrons (12, 13, 14), it is possible to study neutron diffraction also by observation of the transmitted beam (15 to 18), a method impossible for x-rays, since the high ab-

sorption of x-rays precludes this possibility. Neutron transmission as a diffraction method is applicable mainly at wavelengths about 2 to 4 Å where only a few Bragg reflections are active; at still longer wavelengths it is a useful method for study of incoherent scattering.

In comparing neutron with x-ray diffraction it is important to realize that there are serious limitations at present in the newer technique arising from intensity and resolution. In addition, most of the neutron diffraction work has been done with the powder diffraction method, for which the intensity limitation is felt strongly because the scattered neutrons for a single reflection are distributed throughout a complete Debye-Scherrer ring, whereas the detector is at only one point in this ring. Although intensity in the Bragg peak would have a much better ratio to background for single crystals, difficulties also arise there because the samples for the usual diffraction equipment would be so large that serious extinction effects would ensue (19, 20, 21). The large scale of the sample, of course, corresponds to the large scale of diffraction equipment, dictated by the necessity of obtaining sufficient intensity. Recent work (22, 23, 24), however, seems to indicate that samples as large as 1 mm. can be used without serious extinction effects and that the gain in intensity and reduction in background may make the single crystal technique applicable to neutrons.

In addition to diffraction, the optical property of reflection is observed for neutrons with an index,  $n$ , given (4, 8, 19) by the bound coherent scattering amplitude,

$$n^2 - 1 = \lambda^2 N a_{\text{coh}} / \pi, \quad 5.$$

where  $\lambda$  is the neutron wavelength and  $N$  the number of nuclei per cm.<sup>3</sup>. For most materials the scattering amplitude is positive and the index less than unity, corresponding to hard sphere scattering, but for a few, notably hydrogen, the scattering amplitude is negative because of the proximity of a nuclear resonance (9). While refraction can be measured for neutrons (25), the effects are extremely small because of the weak scattering (the index differing from unity by about  $10^{-6}$ ). The critical angle for total reflection, which occurs for materials of positive amplitude, is of the order of 20 minutes of arc for available neutron wavelengths and can be measured with good accuracy (25, 26, 27). The critical angle,  $\theta_c$ , is very simply related to the coherent amplitude,

$$\theta_c = \lambda(Na/\pi)^{1/2}, \quad 6.$$

and this direct relationship makes the critical angle measurement a valuable approach in the determination of several fundamental constants. Because the scattering is in the forward direction, the Debye-Waller factor is unity; furthermore the critical angle is independent of the crystalline structure of the mirror. As a result of these properties the critical angle is a sensitive measure of the coherent amplitude even when extremely large incoherent effects are present (28), as for the neutron-proton scattering.

When the interaction of neutrons with magnetic materials is considered, additional interactions must be taken into account in diffraction and refraction. In the case of diffraction an atomic form factor now enters the structure factor because of the finite spread of the electron shells responsible for the atomic magnetic moment. The form factor arising from the electron distribution is closely similar to the x-ray atomic form factor, but differs slightly because only a few of the electrons are magnetically active (4, 7). An additional angular variation of scattered intensity arises because the fundamental magnetic neutron-electron interaction, a dipole-dipole interaction, is angle-dependent (4). For aligned spins, either in a ferromagnetic or anti-ferromagnetic arrangement, the magnetic scattering is coherent, but for unaligned spins, as in paramagnetic materials, the scattering is incoherent. The coherent and incoherent magnetic scattering manifest themselves in diffraction patterns just as their nuclear scattering analogues.

The effect of the magnetic interaction on the index of refraction is merely to add a term whose sign depends on the orientation of the neutron moment,  $\mu$  relative to the average magnetic induction  $\bar{B}$ ,

$$n^2 = 1 - (\lambda^2 N a_{\text{coh}} / \pi) \pm (\mu \bar{B} / E), \quad 7.$$

with  $E$  the neutron energy (6, 8, 29, 30, 31). The doubly refracting nature of a ferromagnet thus produces two critical angles, a phenomenon useful for the production of polarized neutrons. Any magnetic incoherent scattering has no effect at all on mirror reflection because its average value is zero.

#### NUCLEAR APPLICATIONS

For utilization of the interference effects of slow neutrons in determination of the structure of material, knowledge of the coherent cross sections of the nuclei present in the structure is first necessary. For this reason, measurement of the coherent amplitudes for many materials was a preliminary to actual structural studies. In addition to their use in structural work, several of the coherent amplitudes are of great intrinsic interest in connection with basic nuclear physics. The measurement of these latter has merited special attention.

A series of coherent cross section measurements, obtained by the powder diffraction technique, was reported by Shull & Wollan (32) in 1951. Their work was performed by analyzing simple crystals of known structure, for which the observed amplitudes for the Bragg peaks (the structure factors) could be used to determine the relative coherent amplitudes of the constituents of the crystals. Although diffracted intensities in principle give the coherent amplitudes in an absolute manner, this procedure would be difficult because it would necessitate accurate measurement of the intensity of the diffracted beam and of the incident beam. The measurements instead were of a relative nature only, that is, an unknown amplitude would be determined relative to that of some standard element present in the same crystal. The ultimate standard in the work of Shull & Wollan was carbon, whose

coherent cross section was determined from its total scattering cross section (33, 34). The amplitudes measured by diffraction have in general an accuracy of about 3 per cent, which reaches 1 per cent in a few favorable cases. One difficulty in the determination of coherent amplitudes from diffraction patterns arises from the Debye-Waller factor, which, although well established for elements, is much more uncertain for compounds.

In principle, coherent amplitudes can also be determined directly from observation of the critical angle for total reflection; here no correction is necessary for temperature diffuse scattering as the Debye-Waller factor is unity. The mirror method has limited accuracy, however, because the coherent cross section depends on the fourth power of the measured critical angle; thus, a 1 per cent accuracy in the latter would be necessary to give accuracy comparable to that of the usual powder diffraction work. The early critical angle measurements of Fermi & Marshall (13) were used mainly to obtain the sign of the scattering amplitude, which is given directly by mirror reflection as contrasted to diffraction methods (which are sensitive to the square of the amplitude), but they were not of sufficient accuracy for coherent amplitude determinations. The coherent cross section of beryllium was measured by Harvey, Goldberg & Hughes (25) in an investigation of the accuracy that could be obtained with mirror reflection; here the accuracy reached was 0.5 per cent in the critical angle or 2 per cent in the coherent cross section. Fortunately, balancing techniques are available for mirror reflection, and where these are applicable (for example in the hydrogen and the electron scattering to be described) the attainable accuracy is much higher. The balanced mirror technique was used by McReynolds & Johnson (26) for helium, oxygen, and nitrogen, although the results had an error of about 10 per cent.

Contrasted to the direct measurement of coherent cross sections by neutron diffraction or mirror reflection, an indirect approach based on the total cross section sometimes results in superior accuracy. The total scattering cross section can be obtained readily by a transmission experiment if the neutron absorption is small, for the latter can then be subtracted as a minor correction. When the neutron energy used in the transmission measurement is sufficiently high so that the atom acts as if free during the collision the so-called "free atom cross section" is obtained, which is simply related to the coherent cross section. The free atom cross section is first converted to the value appropriate for a completely bound atom by multiplication by the reduced mass factor,  $(A+1)^2/A^2$ , where  $A$  is the atomic weight (35). The bound atom value obtained in this way comprises the total scattering cross section, from which the coherent component is obtained by subtraction of the incoherent scattering. No subtraction is necessary for a mono-isotopic material of zero spin (carbon and oxygen to all intents and purposes fit this description) because the bound atom and the coherent cross sections are identical.

On first thought it might seem that very high neutron energies would



be necessary to attain free atom behavior, for the energy transferred to the atom is only a small fraction of the neutron energy. However, the availability of many energy states in crystals implies that the free atom cross section is already attained at an energy of a few electron volts (36, 37). Although the cross section at such low energies is close to the free atom value, minor corrections must be made for the Doppler (36) and interference effects (38). The coherent cross section of carbon is one that has been accurately determined from the free atom. Its isotope incoherence is small because the  $C^{13}$  coherent cross section is of very small abundance. The "best values" of the coherent cross sections of oxygen and bismuth shown in Table I also have been obtained recently from the free atom values (39). In the case of bismuth the possibility of spin-dependent incoherence is present, but it was measured (40) by means of extremely long wavelength neutrons and a correction made (0.02 barns) in the conversion from the bound atom to the coherent cross section.

The present best values of the coherent amplitudes are listed in Table I, which is based on the compilation of the Atomic Energy Commission Neutron Cross Section Advisory Group (41). See also the first two supplements, available from Brookhaven National Laboratory, Upton, N. Y. Most of the coherent amplitudes given in this table have been determined by neutron diffraction; they have an error of the order of 3 per cent, except for a few, for example Ni, for which particular effort has resulted in a 1 per cent error. Higher accuracy was obtained from free atom cross sections for C, Be, O, Fe, and Bi. A few of the amplitudes are negative, and in most of these cases the particular resonance whose proximity causes the negative amplitude is known.

The coherent hydrogen amplitude has received special emphasis in the last few years because of its importance to basic nuclear theory. As can be seen from equations 1 and 2, the coherent scattering and the total scattering give the amplitudes for the  $i \pm \frac{1}{2}$  spin states, the triplet and singlet states. These amplitudes, when combined with other low energy data (deuteron binding energy and neutron-proton scattering near 1 Mev), give the ranges of the neutron-proton force for the triplet and singlet configuration (42, 43, 44). Comparison of the latter range with the corresponding proton-proton range then provides an important test of the hypothesis of charge independence of nuclear forces.

The first measurement of the neutron-proton amplitude was accomplished by means of the scattering of slow neutrons from ortho- and parahydrogen (45, 46, 47). The results of this method, in which the coherent scattering is obtained from the parahydrogen cross section, led to a singlet neutron-proton force range that disagreed markedly with the proton-proton range. The Los Alamos results (48) of 1947, which utilized timed cyclotron neutrons, gave  $-3.95 \pm 0.12 \times 10^{-13}$  cm. for the coherent amplitude, corresponding to an  $n$ - $p$  range somewhat closer to the  $p$ - $p$  range but still in disagreement with it.

TABLE I

COHERENT AMPLITUDES OF ELEMENTS AND ISOTOPES

Element or Isotope	$a_{\text{coh}}$ 10 <sup>-13</sup> cm.	Element of Isotope	$a_{\text{coh}}$ 10 <sup>-13</sup> cm.
<sup>1</sup> H	-3.78 ± 0.02	<sup>32</sup> Ge	8.4 ± 0.2
<sup>2</sup> H	6.6 ± 0.2	<sup>33</sup> As	6.3 ± 0.2
<sup>3</sup> He	3.0 ± 0.3	<sup>34</sup> Se	8.9 ± 0.3
<sup>3</sup> Li	-1.78 ± 0.07	<sup>35</sup> Br	6.7 ± 0.2
<sup>6</sup> Li	7 ± 2	<sup>37</sup> Rb	5.5 ± 0.2
<sup>7</sup> Li	-2.52 ± 0.08	<sup>38</sup> Sr	5.7 ± 0.2
<sup>4</sup> Be	7.74 ± 0.04	<sup>40</sup> Zr	6.3 ± 0.2
<sup>6</sup> C	6.61 ± 0.02	<sup>41</sup> Nb	6.9 ± 0.1
<sup>13</sup> C	6.0 ± 0.4	<sup>42</sup> Mo	6.7 ± 0.1
<sup>7</sup> N	9.4 ± 0.2	<sup>45</sup> Rh	6.0 ± 0.3
<sup>8</sup> O	5.81 ± 0.02	<sup>46</sup> Pd	6.3 ± 0.2
<sup>9</sup> F	5.5 ± 0.2	<sup>47</sup> Ag	6.1 ± 0.2
<sup>11</sup> Na	3.51 ± 0.06	Ag <sup>107</sup>	8.3 ± 0.2
<sup>12</sup> Mg	5.35 ± 0.07	Ag <sup>109</sup>	4.3 ± 0.2
<sup>13</sup> Al	3.5 ± 0.1	<sup>50</sup> Sn	6.1 ± 0.2
<sup>14</sup> Si	4.0 ± 0.2	<sup>51</sup> Sb	5.4 ± 0.2
<sup>15</sup> P	5.0 ± 0.1	<sup>52</sup> Te	5.8 ± 0.2
<sup>16</sup> S	3.1 ± 0.1	<sup>53</sup> I	5.2 ± 0.2
<sup>17</sup> Cl	9.8 ± 0.3	<sup>55</sup> Cs	4.9 ± 0.2
<sup>19</sup> K	3.5 ± 0.1	<sup>56</sup> Ba	5.3 ± 0.2
<sup>20</sup> Ca	4.9 ± 0.1	<sup>57</sup> La	8.3 ± 0.2
Ca <sup>40</sup>	4.9 ± 0.1	<sup>58</sup> Ce	4.6 ± 0.3
Ca <sup>44</sup>	1.78 ± 0.07	Ce <sup>140</sup>	4.70 ± 0.08
<sup>21</sup> Sc	10.1 ± 0.4	Ce <sup>142</sup>	4.6 ± 0.2
<sup>22</sup> Ti	-3.3 ± 0.4	<sup>59</sup> Pr	4.4 ± 0.2
<sup>23</sup> V	-0.51 ± 0.06	<sup>60</sup> Nd	7.2 ± 0.2
<sup>24</sup> Cr	3.52 ± 0.03	Nd <sup>142</sup>	7.7 ± 0.3
<sup>25</sup> Mn	-3.7 ± 0.01	Nd <sup>144</sup>	2.8 ± 0.3
<sup>26</sup> Fe	9.52 ± 0.02	Nd <sup>146</sup>	8.7 ± 0.2
Fe <sup>54</sup>	4.18 ± 0.12	<sup>62</sup> Sm <sup>152</sup>	-4.5 ± 0.9
Fe <sup>56</sup>	10.1 ± 0.1	<sup>72</sup> Ta	7.0 ± 0.2
Fe <sup>57</sup>	2.3 ± 0.1	<sup>74</sup> W	4.67 ± 0.04
<sup>27</sup> Co	2.8 ± 0.1	<sup>76</sup> Pt	9.5 ± 0.3
<sup>28</sup> Ni	10.2 ± 0.1	<sup>76</sup> Au	7.62 ± 0.05
Ni <sup>58</sup>	14.4 ± 0.1	<sup>80</sup> Hg	13.2 ± 0.6
Ni <sup>60</sup>	3.0 ± 0.1	<sup>81</sup> Tl	9 ± 1
Ni <sup>62</sup>	-8.7 ± 0.2	<sup>82</sup> Pb	9.6 ± 0.1
<sup>29</sup> Cu	7.5 ± 0.2	<sup>83</sup> Bi	8.63 ± 0.02
<sup>30</sup> Zn	5.9 ± 0.2	<sup>90</sup> Th	10.0 ± 0.1



The coherent hydrogen amplitude was measured in 1948 by Shull *et al.* (49) by means of the diffraction pattern of NaH. The determination was made difficult in this approach by the large amount of spin dependent diffuse scattering (all but two barns of the total bound scattering of about 80 barns), and uncertainty also arose because of the Debye-Waller factor. The result of the experiment, however,  $-3.96 \pm 0.20 \times 10^{-13}$  cm., agreed closely with the Los Alamos work. More recently, Shull & Wollan (32) have published additional work on the hydrogen scattering, in which the temperature diffuse scattering was handled by an empirical method, with a result of  $-4.1 \pm 0.2 \times 10^{-13}$  cm. This change in the result is in the direction of increasing the discrepancy between the  $n$ - $p$  and  $p$ - $p$  ranges.

The mirror method was applied to the hydrogen amplitude in 1950 by Burgy, Ringo & Hughes (50), using a balancing technique. Because of the negative amplitude of hydrogen it was possible to combine hydrogen and carbon in a single mirror, and thus determine the hydrogen amplitude relative to that of carbon by balancing the components to obtain an index of refraction exactly unity. The mirror consisted of liquid hydrocarbons, either single compounds or mixtures. It was found that neutrons could be reflected easily from the liquid surface, in spite of the fact that disturbances of the surface were usually visible. The determination of the hydrogen to carbon ratio of index exactly unity was made by extrapolating observed reflected intensities to zero as the H-C ratio was changed by varying the components. The ratio of the coherent amplitudes was measured in this way to about 0.3 per cent, an accuracy higher than that of the carbon amplitude itself, which is about 0.5 per cent (34). The resulting bound hydrogen amplitude is

$$a_H = -3.78 \pm 0.02 \times 10^{-13} \text{ cm.},$$

where the error includes that in the carbon amplitude.

While the mirror result is lower than the earlier values, it gives an  $n$ - $p$  range, which when combined with other low energy data, is in agreement with the singlet  $p$ - $p$  range and thus consistent with charge independence of nuclear forces (51). This result is also consistent with the binding energy of the triton (52), the mass of the  $\pi$ -meson (53), and the deuteron photodisintegration constants (54). Some recent unpublished results of Squires (55) at the Cavendish Laboratory with the ortho-parahydrogen method have given a coherent amplitude in agreement with the mirror value, thus indicating that the early parahydrogen work must have been affected by an orthohydrogen contamination.

A particularly valuable application of neutron optics has been made in the last few years to the measurement of the electrostatic interaction between the neutron and the electron. In addition to the large magnetic neutron-electron interaction, which we shall consider later, there is expected to be an extremely small non-spin-dependent interaction that is intimately related to meson theory (56 to 59). This interaction will be manifested as a small scattering cross section for neutrons, which, however, is difficult to detect

because it is only of the order of  $10^{-4}$  of the nuclear scattering cross section. The only reason that it can be detected at all is that it is coherent and can be isolated from the nuclear scattering since it exhibits an atomic form factor similar to that effective for x-rays. Several experimental approaches have been applied in the past few years to measurement of the neutron-electron scattering.

The most direct method for study of form factor behavior is the measurement of differential scattering as a function of scattering angle. This approach was followed by Fermi & Marshall (60) who measured the scattering of neutrons from xenon gas at angles of  $45^\circ$  and  $135^\circ$  with the direct beam. Xenon gas was chosen because the closed electron cells ensure that the magnetic interaction between the neutron and the atomic electrons will have no net scattering effect. The angular asymmetry observed, however, was very small and of the same order of magnitude as several necessary corrections, for example the Doppler effect. The results showed that the interaction, expressed as a potential well of range  $e^2/mc^2$  (the classical radius of the electron,  $2.8 \times 10^{-13}$  cm.), had a depth no larger than 5,000 ev, the limit of the experimental accuracy. This upper limit of the strength of the interaction, however, was actually smaller than would be expected from a simple picture of the neutron's intermittent dissociation into a negative meson and a proton. Recently the method of Fermi & Marshall has been repeated by Hamermesh, Ringo & Wattenberg (61) with higher statistical accuracy. Both xenon and krypton gas were used for the electron scattering measurement, and in addition argon gas was studied to check the Doppler correction. The values obtained for xenon and krypton differed somewhat (2900 and 5000 ev respectively) but the average value was 4100 ev with an accuracy of 1000 ev, a major source of uncertainty being the unknown coherent nuclear amplitudes of xenon and krypton.

The form factor variation was studied by Havens, Rainwater & Rabi (62) in another manner, by measuring the total cross section of liquid bismuth as a function of wavelength. The total cross section gives the variation of the integrated form factor of course, which in the wavelength region used, 0.3 to 1.3 Å, varies by about 40 per cent. This form factor variation arising from the neutron-electron interaction results in a cross section change of about 0.1 barn. In the experiment, performed with timed cyclotron neutrons, this small change had to be isolated from others in the same wavelength region amounting to about 0.2 barn (mainly the interatomic interference effects). The value obtained was  $5300 \pm 1000$  ev; the statistical accuracy for this measurement is good, about 500 ev, but uncertainties in the calculated corrections (38) increase the error.

The most recent measurement of the neutron-electron interaction, that of Hughes and co-workers (39), utilizes a balanced-mirror technique. For a coherent scattering amplitude measured by means of the critical angle, the neutron-electron component will be included to its full extent because of the unit form factor. A measurement of the free atom cross section, on the

other hand, gives the coherent scattering with essentially no contribution from the neutron-electron interaction because the form factor is nearly zero. A comparison of the coherent amplitude obtained from the free atom with the mirror result thus gives the full value of the neutron-electron interaction. Because of the averaging property of the mirror any magnetic interaction drops out and the difference between the mirror and free atom measurements is sensitive to the electrostatic neutron-electron interaction only.

The electron scattering is so small that it would be difficult to measure if neutrons were scattered from a single mirror of a high  $Z$  element, say bismuth. The experiment was actually performed by reflecting neutrons from the interface between bismuth and liquid oxygen, the neutron beam, of wavelength  $6.7 \text{ \AA}$ , passing through the bismuth with little reduction in intensity. As the nuclear scattering of oxygen and bismuth are so nearly equal, their effect on the index of refraction practically cancels out, and the observed critical angle is a very sensitive measure of the neutron-electron interaction. The coherent amplitudes of oxygen and bismuth, which must be accurately known in order to obtain the electron scattering from the critical angle for these amplitudes, were determined from the free atom cross sections. Actually only the ratio of the oxygen and bismuth cross sections enter the calculation, and this ratio was measured by a comparison method at a neutron energy of about 8 ev with much greater accuracy than possible for the absolute cross sections. The final result of the mirror experiment was a well depth of  $3900 \pm 400$  ev. where the error includes appreciable uncertainty arising from such constants as the density of liquid oxygen and bismuth.

While the mirror measurement was underway it was pointed out by Foldy (63, 64) that an additional neutron-electron interaction, indistinguishable experimentally from the electrostatic meson effect, would arise from the magnetic moment of the neutron. This Foldy effect, which arises from a relativistic term representing the electric dipole formed by a moving magnetic moment, is 4080 ev in magnitude and produces a neutron-electron amplitude in addition to, and coherent with, the meson-charge effect. Several recent theoretical papers are in substantial agreement with Foldy's result (65, 66, 67). The experimental results for the neutron-electron interaction, however, give a value no larger than this magnetic moment term, so it appears that the electrostatic meson effect is less than a few hundred volts, much smaller than predicted by theory. There does not seem to be any satisfactory way at present to account for the unexpectedly small meson-charge effect (68, 69).

#### ANALYSIS OF HYDROGEN-CONTAINING CRYSTALS

An obvious use of neutron diffraction, and one that was thought to be of great promise when chain-reacting piles were first available, is the location of hydrogen atoms in crystals. Because of the low scattering power of hydrogen atoms for x-rays it is impossible to locate them by this means for

all crystals with the exception of those containing other extremely light atoms. Examination of Table I, however, shows that the neutron scattering power of hydrogen, in contrast to that for x-rays, is of the same order of magnitude as for other atoms. In spite of this obvious advantage possessed by neutrons with regard to the location of hydrogen atoms and the optimism with which the prospect was viewed, there have been only a few examples of hydrogen-containing crystals analyzed by means of neutrons in the five-year period during which neutron diffraction work has been pursued.

The reason for the lack of results is related to several general disadvantages of neutron diffraction relative to x-ray diffraction, and one is particularly applicable to hydrogen. The latter disadvantage arises from the large amount of spin-dependent incoherent scattering of hydrogen, which makes accurate measurement of coherent peaks difficult. Substitution of deuterium for hydrogen in crystals has been of some help in this connection, but deuteration is itself an added complication, of course. The general disadvantages of neutron diffraction are consequences of the present-day low intensity and poor resolution relative to x-ray standards. The intensity available in a typical neutron diffraction apparatus is quite low compared to x-ray equipment, the flux density of neutrons incident on the crystal under analysis being lower by a factor of a million or more compared to the flux density of x-ray photons. Also, the wavelength resolution present in the beam incident on the crystal under analysis has a wavelength spread of several per cent (14, 70, 71, 72) compared to the monochromatic x-ray emission lines used as sources.

A review of the published results on location of hydrogen in crystals shows that in most cases the work is a verification of structures already postulated from incomplete x-ray information, often combined with rather indirect evidence of other types. Usually the basic structure of the heavy atoms is one well determined by x-rays and the detail, for example the precise coordinates of the hydrogen atoms, is then fixed by the neutron diffraction pattern. An early example of the location of hydrogen by neutron diffraction is afforded by the analysis of NaH by Shull *et al.* (49). These studies, which, as we have seen, were also used for a determination of the hydrogen amplitude, showed that NaH possessed the NaCl structure; this seemed likely because x-ray analysis had already shown that LiH had the NaCl structure also (73). The NaH could not be analyzed by x-rays because of the great difference in scattering power of Na and H for x-rays, but the correctness of the assumed structure was easily established by the structure factors of the neutron pattern.

An example of a structure in which several alternative postulated hydrogen arrangements could be tested is that of ice, which was studied by Wollan, Davidson & Shull (74), using "heavy ice,"  $D_2O$ . The poor resolution inherent in neutron diffraction resulted in a failure to resolve many of the Bragg peaks in the powder pattern. The predicted peak intensities calculated for the various models were sufficiently different, however, so that

a unique identification could be made on the basis of the peaks that were resolved. It was shown that the Pauling model (75) was the only one that correctly predicted the observed structure factors. This model of ice is tetrahedral with one hydrogen atom (two "half-hydrogen" atoms) on the lines joining each two oxygen atoms.

The basic structure of ammonium chloride is well known from x-ray analysis (76), but no information was available from this work on the position of the H atoms in the ammonium ion. The location of the hydrogen atoms in the low temperature phase of this compound was studied both at Chalk River by Goldschmidt & Hurst (77, 78) and at Oak Ridge by Levy & Peterson (79). The difficulty of the neutron diffraction study of hydrogen location is illustrated by the uncertainty present for some time in the results. At first the Chalk River work (77) indicated ordering of the  $\text{NH}_4$  ions in the low temperature phase (below  $-30^\circ\text{C}.$ ) but later results at Chalk River (78), as well as the Oak Ridge studies (79), revealed an orientational disordering of the ammonium ions. It was necessary to use the deuterated compound for the powder diffraction work carried out at Chalk River. At Oak Ridge the deuterated compound was also used for the powder work, but it was found possible to obtain essentially the same final results with a small single crystal containing hydrogen rather than deuterium.

During the last year a few more diffraction results on hydrogen location have been reported. For example, Rundle, Shull & Wollan have recently published an analysis, based on neutron and x-ray diffraction, of thorium and zirconium hydrides (80). The results of the neutron work confirmed the body-centered tetragonal structure that had been suggested by the x-ray analysis, and in addition gave the accurate coordinates of the hydrogen atoms. The position of hydrogen in potassium bifluoride was determined by Peterson & Levy (81), who showed that the hydrogen atom was equidistant from the F atoms in the  $\text{HF}_2$  ion, which is linear. The form of the Debye-Waller factor necessary to explain the observed intensities revealed that the incoherent scattering was related to a rotational oscillation of the bifluoride ion. The deuterated compound was investigated by powder diffraction, but better results were actually obtained from a single crystal without deuteration.

The complementary nature of x-ray and neutron analysis for many crystals is illustrated by the results that have been obtained to date by neutron diffraction. The basic structure of the heavy atoms can be determined quite easily by standard x-ray techniques, then the hydrogen atoms, invisible in general to x-rays, can be located by neutrons. The use of single crystals, as already mentioned, indicates that deuteration is not essential for study of hydrogen-containing crystals. Another advantage follows from the use of single crystals because the sample size is much smaller than for powder diffraction and the ratio of diffuse scattering to peak heights is thereby reduced greatly (22, 23, 24). The decrease in diffuse scattering which results from the reduction in sample size, is, of course, of great value for hydrogen analysis.



## MAGNETIC SCATTERING OF NEUTRONS

Neutron optics has proven to be of great value to the study of magnetic structures because the dipole moment of the neutron has made possible direct investigations of atomic moments. Neutron scattering measurements give the orientation and location of the magnetic moments in a material just as x-rays make possible the location of the atoms themselves. In a manner analogous to structure studies by neutron diffraction, it was first necessary to investigate the fundamental characteristics of magnetic scattering of neutrons in order to put the structure investigations on a firm basis. Whereas the preliminary nuclear scattering measurements consisted of scattering amplitudes that could not be predicted by theory, the principal magnetic problem was a verification of the theoretical formulas for the amplitude of the magnetic interaction. Once the theoretical formulas are fully justified, the magnetic scattering amplitudes can be calculated easily from the atomic magnetic moments, unlike the nuclear amplitudes, which always require measurement.

For several years after the first discussions of magnetic scattering, some uncertainty persisted concerning the fundamental interaction between the neutron and the atomic magnetic moment, an uncertainty that was reflected in the evaluation of the magnetic scattering amplitude. Thus the point-dipole interaction first used by Bloch (82) led to a different angular variation for the magnetic amplitude than did the Dirac (or Amperian) current used by Schwinger (83) and Halpern & Johnson (4) for the "shape" of the neutron moment. These two viewpoints actually correspond (30) to the assumptions that  $H$  (dipole assumption) or  $B$  (Dirac current) represent the field effective for the neutron in passage through a ferromagnet.

The early experiments on magnetic scattering, such as the transmission in magnetized iron used for production of polarized neutrons (discussed later), or the small angle scattering of neutrons in magnetic materials (84), showed that the correct formulation was probably that based on the Dirac current, or effective field  $B$ . The correctness of this view was shown in a direct manner, however, by a mirror reflection experiment of Hughes & Burgy (85). This experiment revealed the presence of two distinct critical angles for reflection of neutrons from magnetized iron mirrors, thus proving that  $B$  is the correct effective field because  $H$  would lead to the appearance of only one critical angle, corresponding to the nuclear scattering alone. The presence of two critical angles also has the interesting consequence that it is a direct demonstration of the fact that the neutron spin is one-half (86).

Although the mirror experiments showed the validity of the Dirac current formulation there were additional theoretical questions concerning the validity of the derivation of the index of refraction in a magnetic material. Thus, while the equation already given for the index, equation 7, definitely was substantiated by the magnetic mirror results (85), questions concerning its derivation have been the subject of several publications since that time (8, 30, 31, 87).

The variation of amplitude with magnetization direction was measured

directly by Shull, Wollan & Koehler (88) as a test of the correct interaction form, using powder diffraction from magnetite,  $\text{Fe}_3\text{O}_4$ . The scattered intensity in the (111) Bragg peak was measured with the sample magnetized in various directions, and the angular variation obtained showed definite agreement with the Dirac assumption rather than with that of the point dipole interaction. The excellent agreement shows that the angular variation is accurately predicted by theory (4).

A complicating factor in magnetic analysis by diffraction, which does not occur for nonmagnetic crystals, is the magnetic form factor arising from the distribution of the magnetically active electrons (those of the 3d shell in iron, for example). This form factor, which enters into the calculation of the amplitudes to be inserted in the structure factors, is unfortunately more difficult to estimate than the analogous atomic form factor for x-rays. The difficulty results from the fact that the distribution of the magnetically active electrons alone is more uncertain than that of the entire structure of orbital electrons, which is effective for x-rays. As the form factors used by Halpern, *et al.* (6) and later by Hamermesh (7) had predicted magnetic effects lower than those observed in neutron polarization experiments (89), they seemed to contain a numerical discrepancy although they were qualitatively correct. Somewhat later, a quantitatively different form factor was used by Steinberger & Wick (90), which gave good agreement with the observed neutron polarization results.

The atomic form factor was checked directly by neutron diffraction experiments of Shull *et al.* (88), in which the amplitude of iron was measured in different Bragg peaks. The angular variation resulting from the Debye-Waller factor was corrected for by calculation and the remaining scattering divided into the nuclear and magnetic components, the latter exhibiting an angular variation in good agreement with that calculated from the form factor of Steinberger & Wick. The experimental results that we have reviewed concerning the correct interaction form as well as the magnetic atomic form factor justify the theoretical equations and demonstrate that structure factors for magnetic scattering can be calculated with confidence from the atomic magnetic moments.

Magnetic scattering phenomena have been applied with significant results in the last few years to the investigation of ferromagnetic, anti-ferromagnetic, and paramagnetic materials. These have been studied to some extent by transmission for long wavelength neutrons, although most of the results have been obtained by the diffraction technique. The methods used in the diffraction work are closely similar to those applied to nonmagnetic crystals. The magnetic scattering from aligned spins, that is from ferromagnetic or anti-ferromagnetic samples, will be coherent; that from unaligned spins, paramagnetic samples, will be incoherent. Thus, magnetic scattering from the unaligned spins of paramagnetic materials with the attendant random variation of scattering amplitudes is quite similar to the spin-dependent incoherent scattering that occurs for nuclei. The additional magnetic angular variations complicate the neutron diffraction patterns



relative to those of nonmagnetic materials, but it is just these complications that make it possible to gain information on the distribution and orientation of the atomic magnetic moments.

An example of magnetic structure analysis is the work of Shull, Wollan & Koehler (88) on magnetite, which is ferromagnetic but with a weaker magnetization than iron. This weakening of the ferromagnetism is caused by the alignment of some of the moments antiparallel to the majority, in other words an anti-ferromagnetic arrangement. The actual detailed structure was shown by the powder diffraction pattern to correspond to one postulated by Néel (91), the so-called "ferrimagnetic" structure, with anti-ferromagnetic coupling of the octahedral and tetrahedral iron atoms. In computing the intensities expected from this structure it was necessary to take into account the presence of iron atoms of two states,  $S=2$  and  $5/2$ , hence of different magnetic scattering amplitudes. The intensities were studied at sample temperatures both above and below  $80^\circ\text{K}$ ., but no changes were observed, showing that the orientation of magnetic moments does not change at this temperature even though a discontinuity in gross magnetic structure does occur. The ferrites, of which magnetite is an example, are now undergoing extensive study by neutron diffraction at several laboratories, although at the time of this review few reports have appeared (92, 126). An analysis of the ferromagnetic material  $\text{Mn}_2\text{Sb}$ , performed by methods similar to those used for magnetite, has recently been reported by Gingrich, Shull & Wilkinson (93).

The magnetic structure of  $\text{MnO}$  was verified by neutron diffraction in work of Shull *et al.* (94, 95). In this material the anti-ferromagnetic arrangement is complete below  $120^\circ\text{K}$ ., that is, the magnetic moment exhibited by macroscopic samples is zero. Since the anti-ferromagnetic arrangement in  $\text{MnO}$  is one in which alternate spins are antiparallel, the resulting diffraction pattern is particularly simple. There is in effect a magnetic unit cell twice the size of the chemical unit cell, hence peaks are observed in the diffraction pattern corresponding to a lattice spacing twice that observed for x-ray diffraction. It was found by Shull *et al.* that these peaks, which were distinct at low temperature, broadened as the Curie point ( $120^\circ\text{K}$ .) was passed but were still observable at room temperature. The persistence of the broad peaks reveals a short range ordering of spins well above the Curie point. In another anti-ferromagnetic materials, however, such as  $\text{MnF}_2$  (95),  $\text{NiF}_2$  (96) and  $\text{MnO}_2$  (97), the peaks disappeared above the Curie point, and typical paramagnetic diffuse scattering was observed.

The scattering of neutrons from paramagnetic materials is particularly simple in the ideal case of completely disordered spins, for such scattering is incoherent and the only angular variation comes from the form factor. Thus for a given  $S$  value and spatial distribution of the magnetic electrons the angular distribution will be an easily calculable, smoothly varying function with no coherent peaks. The angular variation is useful as a verification of the theoretical form factor, a verification that has been accomplished

both by transmission measurements at long wavelengths (98, 99) and by powder diffraction (95, 101).

The total cross section, which gives the integral of the form factor, was measured with cyclotron neutrons by Ruderman (98) and recently by Smith *et al.* (99) with the Brookhaven slow chopper. Both investigations revealed the expected variation of the integral form factor with wavelength. Whereas the cyclotron results reached an integrated form factor of about 0.7, the slow chopper work, in which wavelengths as long as 15 Å were used, extended well into the region where the form factor is unity and the paramagnetic cross section therefore constant. The theoretical wavelength variation was observed for  $\text{MnF}_2$  both with the cyclotron and the slow chopper, but departures from theory were found for  $\text{MnO}$ . These departures are related to the short range anti-ferromagnetic order in  $\text{MnO}$  above its Curie point mentioned earlier.

In the powder diffraction measurements the form factor of the diffuse paramagnetic scattering is investigated directly and, as is done with x-rays, the angular variation can be converted to a radial distribution of electrons by Fourier analysis. The results of this analysis in the work of Shull *et al.* (95) showed that for  $\text{MnF}_2$  the radial distribution of electrons in the  $\text{Mn}^{++}$  ion was in good agreement with a theoretical calculation of Dancoff (100). The results for  $\text{MnO}$ , however, were anomalous as we have seen, the broad coherent peaks indicating a tendency toward the anti-ferromagnetic arrangement, which is complete below the Curie point. The paramagnetic scattering in  $\text{MnO}$  and  $\text{MnF}_2$  was also studied by Bendt (101), who measured the intensity of scattered neutrons as a function of wavelengths (1 to 5 Å) and found evidence for more short range order in  $\text{MnO}$  than in  $\text{MnF}_2$ .

Both the diffraction and transmission results indicate that the spins in  $\text{MnO}$  are not free to rotate but are ordered at temperatures well above the Curie point. This short range order results in the scattered neutrons being concentrated near the Bragg reflections in diffraction, while in the transmission work the cross section does not level out with increasing wavelength but instead continues to rise. This latter behavior is evidence for the absorption of energy by the neutrons in amounts large compared to the neutron energy, in contrast to the elastic paramagnetic scattering of disordered spins. An extreme case of this inelastic scattering in a paramagnetic material has been observed by Palevsky, Carter & Hughes (102) in iron above the Curie point, for which the cross section for long wavelengths is proportional to  $\lambda$ . The strict proportionality to  $\lambda$  shows that there is very little elastic paramagnetic scattering in iron above the Curie point and, furthermore, that the scattering is always associated with energy gain by the neutron. Thus, even though iron loses its ferromagnetic properties above the Curie point, all of the spins are locked strongly enough so that the energy involved in their flipping is large compared to the neutron energy, which is of the order of  $10^{-3}$  ev.

The scattering of neutrons by magnetic crystals seems likely to be of

great value as an aid to the understanding of the fundamental nature of magnetism. An example of this function is afforded by the finding that neutrons scatter from iron as if the magnetic moment of each atom is 2.2 magnetons, rather than an average of 2.2 with integral values being associated with the actual atoms. While this result seems to indicate that integral spins are not associated with individual atoms, as is assumed in one form of the theory (103), the result is not clear-cut. There exists the possibility that only integral spins exist for individual atoms, yet in a pattern that changes sufficiently rapidly so that the neutron would be affected only by the average value at a particular lattice site (104). Investigations of the localized magnetic moments have been carried out by Shull & Wilkinson (105) for the transition elements, V, Cr, Mn, Cb, Mo, and W. While these investigations of the fundamentals are still in the early stages, they promise to be of great importance to magnetic theory.

The fact that the scattering amplitude for magnetic materials is two-valued has been used to separate the neutron spin states, that is, to produce beams of polarized neutrons. Polarized neutrons were first produced by transmission through magnetized iron (89, 106 to 110), in which those neutrons for which the magnetic scattering amplitude is positive have the larger total scattering cross section and hence will be more readily scattered out of a beam. Transmission in sufficiently thick pieces of magnetized iron would therefore produce highly polarized neutron beams, were it not for the unfortunate fact that a few magnetic domains slightly out of line with the applied field cause a precession of the neutron spins and a resultant serious depolarization (5). The use of large thicknesses of iron of course also implies a great reduction in intensity. References to work prior to 1940 are given by Alvarez & Bloch (106).

Polarization by transmission was used with cyclotron neutrons for the measurement of the neutron spin (106, 111) and as a study of the process of polarization itself (107 to 110). The high intensity of polarized neutrons available from the pile was used by Arnold & Roberts for a determination of the neutron moment (112) and by Hughes, Wallace & Holtzman for a detailed study of the process of polarization by transmission (89). In the latter work it was possible to obtain a polarization as high as 50 per cent but this necessitated transmission through samples as large as 6 cm. of highly magnetized iron. In the experiments the polarization of a beam is measured by transmission through a second piece of magnetized iron, the analyzer, in which the change of transmission with direction of magnetization can be related to the polarization.

The doubly refracting nature of iron leads to another method for separation of spin states, that of reflection from magnetized mirrors. For monochromatic neutrons incident on a magnetized iron mirror at an angle intermediate to the two critical angles, only that spin state for which the nuclear and magnetic amplitudes are positive will reflect; as a result the reflected beam will be completely polarized. Complete polarization will not result for

the entire Maxwell distribution, for some neutrons of both spin states will reflect, the fraction being much larger for the spin state of higher index. It was pointed out by Hamermesh (113) that complete polarization could be attained by reflection from cobalt without the loss in intensity resulting from monochromatization. As the nuclear scattering is less than the magnetic in cobalt, only one index will be less than unity (equation 7), hence only one spin state will reflect regardless of the wavelength and critical angle. Polarization by reflection at both iron and cobalt mirrors was studied by Hughes & Burgy (85), who showed that complete polarization was attained with the latter, the polarization being measured by reflection at a second mirror. The change in reflectivity of this mirror resulting from reversal of its magnetization direction is simply related to the polarization of the incident beam.

The dependence of the structure factor for Bragg reflections on spin direction makes diffraction a possible method for polarization as well. As the nuclear amplitude is isotropic while the magnetic amplitude has the magnetic form factor, it is possible that in a certain reflection the magnetic and nuclear amplitudes will be equal. In this reflection one spin state will have double the nuclear amplitude, while the other is of zero amplitude. This method of polarization, first suggested by Fermi (114), was later demonstrated by Shull *et al.* (88, 115). The crystal used in the experiment was magnetite, for which the magnetic scattering is almost exactly the same as the nuclear for the (220) reflection. The polarization of the diffracted beam was shown to be complete within experimental error by analysis in a transmitting block of magnetized iron.

The various methods of production of polarized neutrons differ somewhat in the characteristics of the polarized beam produced and hence have corresponding differences in applicability. For example, the mirror reflection involves beams collimated to a few minutes of arc and in addition is effective for long wavelength neutrons. The diffraction method, on the other hand, produces monochromatic neutrons but only in the region for which diffraction is possible, that is for wavelengths less than the crystal cutoff. Transmission requires the least in collimation, but the attendant initial high intensity is drastically reduced for any polarization larger than a few per cent.

Polarized neutrons have not been used to date for fundamental nuclear experiments to any extent because polarization of the nuclei is also necessary in general. The depolarization of a beam that results from spin-dependent scattering has been used to measure the latter (116), but the method does not give results as accurate as those which can be obtained directly by comparing the coherent with the total cross section. Progress in the polarization of nuclei has been made recently (117, 118), and polarized neutrons will be of definite applicability in this connection. Capture of polarized neutrons by nuclei, while resulting in a nonuniform population of magnetic substates (hence, polarized nuclei), does not produce an angular asymmetry of capture  $\gamma$  radiation (119, 120).

Certain magnetic properties, especially those relating to domain structure, are particularly amenable to investigation with polarized neutrons because the depolarization of a beam is a sensitive measure of domain size and orientation. Experiments of Burgy *et al.* (121) on depolarization of neutrons in thin samples showed good correlation between the domain size measured by depolarization and the grain size as determined by metallographic methods. This comparison was made for a number of samples that had received various metallurgical treatments, such as severe cold-rolling. The sensitivity of neutron polarization to unaligned domains was used by Hughes, Wallace & Holtzman (89) in a study of the approach to saturation of highly magnetized iron. This work showed deviations from the theoretical prediction (departure from saturation  $\propto H^{-2}$ ) for magnetizing fields of the order of 10,000 oersteds.

#### OTHER APPLICATIONS OF NEUTRON OPTICS

Because of the limited intensity and resolution available for neutron diffraction studies, the use of neutrons instead of x-rays is indicated only when there is information to be gained that is unattainable by x-ray analysis. In addition to the investigations of hydrogen-containing and magnetic crystals, neutron analysis has been used as an adjunct to x-rays for several other structural problems.

Like hydrogen, other light atoms are difficult to locate by x-rays, especially when present in crystals containing heavier atoms. Neutrons are of possible use for analysis of such crystals, and if the light element does not have high incoherent scattering it is possible that the analysis is much easier than with x-rays. The study of intermetallic compounds by Koehler *et al.* (122) is an example of the location of light atoms in the presence of heavy metal atoms. The compound studied,  $MBe_{13}$  (where  $M$  is a heavy metal), already been investigated by x-rays but the results were somewhat uncertain because of the small scattering power of Be. The neutron diffraction pattern showed that the structure is face-centered and isomorphic with  $NaZn_{13}$ , a compound that had been investigated satisfactorily with x-rays (123) because the difference in mass of the atoms was not extreme.

In some crystals, analysis is aided by large differences in the scattering amplitudes of the components, for example in ordered compounds, for which the intensity of the superlattice lines depends on the difference in scattering amplitudes. Thus the superlattice lines from  $Cu_3Au$  can be studied by x-rays, for the difference in atomic weight causes an appreciable difference in x-ray scattering amplitude. On the other hand, the x-ray diffraction patterns of  $FeCo$  and  $Ni_3Mn$  cannot be measured by x-ray diffraction. The neutron powder diffraction patterns of these latter two materials, measured by Shull & Siegel (124), show the superlattice lines clearly, because of the unusually great difference in the amplitudes of the components of both materials. Another example of the use of neutron diffraction for materials in which the difference in scattering amplitudes is exploited is the analysis by Bacon (125)



of spinel,  $\text{MgAl}_2\text{O}_4$ . In this case the difference in scattering amplitudes of Mg and Al, although of similar atomic weight, showed that the so-called "normal" instead of the "inverse" structure, was correct. Later measurements of Bacon & Roberts (126) extended this work to solid solutions of magnesium ferrite ( $\text{MgFe}_2\text{O}_4$ ) in  $\text{MgAl}_2\text{O}_4$ .

Another difference between x-ray and neutron scattering was used by Bacon (127) in an investigation of the anomalous intensity pattern observed in the x-ray analysis of graphite. The x-ray diffraction pattern had been interpreted as the result of either an anomalous Debye-Waller temperature factor or a nonspherical electron distribution in the carbon atoms. As only the former hypothesis would affect neutron diffraction, the finding of Bacon that the neutron pattern was normal showed definitely that the hypothesis of a nonspherical electron distribution was correct.

In reviewing the uses of neutron optics we have so far considered only crystalline materials, although there has been some application of neutron diffraction to the analysis of gases and liquids. While the methods are very much the same as standard x-ray techniques, there is an advantage in principle for neutrons because the isotropic nuclear form factor implies that the intensity will not decrease with increasing scattering angle. The diffraction patterns of liquid sulphur, lead, and bismuth were obtained by Chamberlain (128) with diffraction equipment in which a range of wavelengths was utilized, thus giving an increased intensity compared to a monochromatized beam. The results of this work agreed with x-ray analysis of these liquids but did not show any detailed structure not revealed by x-rays. Similar results were later obtained with the same equipment by Czyzak & Wattenberg in a study of heavy water (129). In the case of vitreous silica, however, investigated both by diffraction methods at Oak Ridge (130) and by transmission of long wavelength neutrons at Columbia (131), more peaks were observed than for x-rays.

The neutron diffraction patterns of several gases, studied at Chalk River (132, 133, 134), are in excellent agreement with a semiclassical calculation in which the energy changes resulting from inelastic scattering are neglected (135). For most of the gases studied, namely  $\text{H}_2$ , F, N, and O, the principal results were coherent amplitudes of the nuclei involved. In the case of  $\text{CF}_4$ , however, the C—F bond length also was measured.

As the penetrating power of neutrons is usually high compared to that of x-rays, it is possible that neutrons will be useful in the investigation of properties in the interior of macroscopic samples. An example is furnished by the investigations of cold-worked brass by Weiss *et al.* (136). The broadening of peaks observed with x-rays was shown to be a result of the distortion of crystal grains. The penetrating power of neutrons also makes it possible to observe the small angular deviations resulting from multiple refraction (or diffraction for extremely small particles) in the particles of a powder sample (137, 138), or in the domains of an unmagnetized ferromagnet (84). Although small angle scattering results have been useful as examples of the theory

of neutron refraction and diffraction (139, 140), they have not given structural information as yet.

The effect of lattice vibrations in causing a decrease in coherent scattering is taken into account in x-ray diffraction by the Debye-Waller factor (3), and this factor is also used for the same purpose in neutron diffraction (6, 19, 141, 142). There is a fundamental difference, however, between the lattice vibration scattering of neutrons and x-rays, for the energy changes involved, which are negligible in x-ray scattering, are comparable with the incident energy for neutrons. The occurrence of large energy exchanges implies that their measurement can be used to gain direct information on the lattice vibrations. Most of the studies of lattice vibration scattering have utilized "cold" neutrons, of wavelength beyond the crystal cutoff, for which no coherent scattering is observed.

At long wavelengths, the residual cross section arises from capture, isotopic incoherence, spin-dependent incoherence, and lattice vibration scattering. The various components are identified by particular characteristics, the last, for instance, being the only temperature-sensitive scattering. Because the energy gained by a long wavelength neutron in the inelastic scattering is large compared to its own energy, the cross section is proportional to  $\lambda$ ; in the low energy region where the " $\lambda$  law" holds the theoretical calculation is somewhat simplified.

The inelastic scattering of very cold neutrons has been studied with the Brookhaven slow chopper for graphite, beryllium, bismuth, and iron (143 to 146) and with velocity-selected cyclotron neutrons at Cambridge, England (147, 148, 149), for magnesium, aluminum, nickel, and iron. For all of these materials, except graphite and iron, the experimental results are in good agreement with the theory (150 to 154) which is based on a Debye frequency spectrum. For graphite (143), the layer structure leads to a discrepancy with the Debye frequency spectrum, a discrepancy that is similar to that observed for the graphite specific heat (155). For iron (145, 146, 149, 156), an excess inelastic scattering is observed that increases rapidly with energy and levels off above the Curie point. We have already mentioned the connection between this finding and the short range order in iron above the Curie point; below this temperature the excess scattering has been attributed to "spin waves" (157).

In the experiments described, the energy gain of the neutrons is not measured, except in the sense that the  $\lambda$  law proves that the gain is large compared to the neutron energy. Some results are now available on the more difficult procedure of measurement of the actual energy gain. Brockhouse & Hurst (158) at Chalk River have measured the energy change by means of transmission in thin cadmium, using 0.35 eV incident neutrons, monochromatized with a NaCl crystal. At Harwell, Egelstaff (159) used an incident beam of lead-filtered neutrons and detected the gain in energy by transmission in lithium. Lowde (160), at the same laboratory, has demonstrated that the neutrons found near but not in the Bragg peaks in the diffraction



pattern of iron have an energy different from that of the incident neutrons, those on one side of the peak exhibiting an energy gain, those on the other side an energy loss.

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## THE STANDARDIZATION OF NEUTRON MEASUREMENTS<sup>1</sup>

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This chapter will be concerned primarily with the techniques for the relative and absolute measurement of neutron flux, neutron density, and the number of neutrons emitted by a source. The more important recent developments will be emphasized and the current status of the art will be reviewed. In 1952, there were available in the laboratory neutrons of energies ranging from a fraction of an electron volt to approximately 400 Mev. The techniques employed in general depend upon the energy of the neutron. Consequently, this chapter is divided into sections on absolute and relative measurements for three different neutron energy regions and a section containing some general remarks which hold for all energy neutrons.

All neutron measurements can be considered to be included in the above categories; obviously some limitations had to be placed on the material to be discussed in this review. It was decided to limit detailed consideration to those techniques or developments which permit one to obtain better precision, to make measurements more readily, or to extend the range of neutron measurements. For those who are unhappy with these limitations it is to be pointed out that the subject of neutron detection up to 1950 has already been reviewed by Jordan in Volume I of the *Annual Review of Nuclear Science* (47). Since then the main developments in neutron detection have resulted from scintillation detector studies. The most useful of such developments which will not be discussed further seem to be in the work of Hornyak (38), Schenck (71), Allen (4), and Poole (65). Fortunately for those in the field of neutron physics, two very useful books have appeared, "Pile Neutron Physics" by Hughes (41) and "Experimental Physics, Vol. II" with the sections on neutrons by Feld (26). Both of these books discuss at some length the methods of neutron detection.

The importance of the subject of neutron dosimetry for the protection of neutron physicists made the author feel that some remarks should be made despite the above limitations on the scope of this chapter. Rossi (70) points out that the determination of neutron flux is not the only problem in neutron dosimetry; the evaluation of the physiological effect of the different energy neutrons is equally important. This latter problem is very much complicated by the presence of  $\gamma$ -rays in almost all sources of neutrons.

<sup>1</sup> The survey of the literature pertaining to this review was concluded in February, 1953.

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For those interested in neutron dosimetry there are two articles available by Moyer (61), and Hughes [(41) Chapter XI] which are, unfortunately, much too brief.

#### GENERAL REMARKS

The most frequent type of measurement is one in which a relative flux or relative yield of neutrons is measured. However, when it is desired to change from ratios to absolute values, the absolute value of a flux or of a neutron source strength is needed.

In very few cases can the interpretation of a neutron measurement be made without a knowledge of the energy of the neutrons being employed. Therefore, the subject of determining the energy distribution of neutrons plays an important part in almost all neutron measurements. Since the techniques and problems arising in such measurements are sometimes rather different from those of other neutron measurements, they warrant separate treatment. Generally, those who make such measurements obtain only the relative energy distribution as the normalization would require an absolute measurement.

The problems that arise and the accuracies obtainable for relative and for absolute measurements are different. Over some energy regions the important developments in the last few years have been directed mainly towards obtaining a precision of a few tenths of a per cent in relative measurements. By comparison, absolute measurements still have errors of the order of 4 per cent. This latter situation can be understood in terms of (a) our knowledge of neutron cross sections, and (b) our ability to determine absolute counting rates.

Except for the associated particle technique and some methods using chain reacting piles, one cannot determine an absolute flux or source strength without the knowledge of a cross section. Therefore, generally the value obtained can be no more accurate than the cross section employed. An investigation of the accuracy to which neutron cross sections are known in any energy region will, in general, tell one the limit to which one can hope to make an absolute measurement. With respect to the measurement of absolute counting rates, many advances have been made in the past decade in other fields of nuclear physics. Several of the important developments during the last few years in establishing better neutron standards have arisen from the application of these advances to neutron measurements.

It is to be noted that many of the problems encountered in obtaining high precision are not specific to one type of neutron measurement. Consequently, techniques developed for decreasing the uncertainties in low-energy neutron measurements are likely to be of assistance to those working at higher energies and vice versa.

#### ABSOLUTE MEASUREMENTS ABOVE 15 MEV

New high-energy accelerators have extended the energy range of neutrons



available in the laboratory. The highest energy neutrons from synchrocyclotrons are about 400 Mev, observed by Goodell *et al.* (30), Fox *et al.* (28), and DeJuren (24). The former detected the neutrons by means of the recoil protons they produced, and DeJuren employed a bismuth fission chamber. High-energy neutrons present in cosmic rays have been studied by the charged particle stars they produced in nuclear emulsions [see Bernardini, Cortini & Manfredini (12)].

At high energies the best absolute neutron measurements have been made by counting the protons which recoil from the elastic collision of neutrons in a hydrogenous target. The recoil protons are detected in a telescope consisting of at least three counters, the last of which is 30 or more centimeters from the hydrogenous target. The majority of people have used scintillation counters; however, proportional counters have been used by Hadley *et al.* (33) and by Cassels *et al.* (20, 78). The energy of the recoil protons is determined by some modification of a range measurement.

The difficulties involved in accurately measuring a neutron flux can be understood by considering the individual factors that determine the recoil proton counting rate. If a flux of neutrons,  $\phi(E_N)$ , hits an infinitely thin hydrogenous target, the counting rate in the proton detecting system will be

$$N_H \frac{d\sigma(\theta)}{d\omega} \Delta\omega \frac{d\phi(E_N)}{dE_p} \Delta E_p F(E_p) \quad 1.$$

$N_H$  is the total number of hydrogen atoms in the beam.  $\theta$  is the angle the proton detector makes with the neutron beam.  $d\sigma(\theta)/d\omega$  is the differential neutron scattering cross section expressed as a function of the angle of the proton recoil.  $\Delta\omega$  is the solid angle subtended by the proton detector.  $[d\phi(E_N)/dE_p]\Delta E_p$  is the flux of neutrons with energies  $E_N$  which will produce recoil protons with energies between  $E_p$  and  $E_p + \Delta E_p$  in the solid angle  $\Delta\omega$ .  $F(E_p)$  is the fraction of the protons in solid angle  $\Delta\omega$  which are actually counted by the telescope.

Obviously, the accuracy of the value of the flux obtained depends upon how well one knows or can determine the other factors in expression 1.  $N_H$  is generally the only factor with a negligible error; each of the other factors is discussed below.

$d\sigma(\theta)/d\omega$ .—For neutrons with energies less than 290 Mev, scattering is effectively the only process in a collision between a neutron and a proton. Therefore one can normalize relative measurements of  $d\sigma/d\omega$  to the total cross section which is more readily measured by an attenuation measurement. The errors which arise in obtaining  $d\sigma/d\omega$  in this way are discussed by Guernsey, Mott & Nelson (31). At the present time the best values of  $d\sigma/d\omega$  at high energies have an uncertainty of at least 4 per cent.

$\Delta\omega$ .—If one works with expression 1 in the laboratory system,  $\Delta\omega$  should be calculable from the physical size of the detectors, their distance from the hydrogen target, and the angular spread in the original beam

of neutrons. However, Chamberlain, Segrè & Wiegand (21) point out that an uncertainty in  $\Delta\omega$  can arise from a lack of uniformity of response of the detector (over the surface of the detector). Chamberlain *et al.* put an uncertainty<sup>3</sup> of 3 per cent on their value of  $\Delta\omega$ .

$\Delta E_p$ .—Two methods have been employed for setting the value of  $\Delta E_p$ ; one is a differential range measurement and the other is a differential pulse height modification of a range measurement.

In the differential range measurement, the proton is required to stop in a detector of thickness  $\Delta X$ . Selove, Strauch & Titus (73) and Bodansky & Ramsey (16) use an anticoincidence crystal detector at the back of their telescope to be sure that the proton has stopped in  $\Delta X$ . In this method  $\Delta E_p$  is just  $\Delta X(dE/dX)$  where  $dE/dX$  is the rate of ionization energy loss for energy  $E_p + \frac{1}{2}\Delta E_p$  (if  $\Delta E_p$  is small). In the differential range measurement the uncertainties in  $\Delta E$  which are considered negligible are: the uncertainties in  $dE/dX$ , the uncertainty in the depth of penetration of a particle into a detector in order for the particle to be recorded, the obliquity of the protons, and the range straggling. (The range straggling is about 1 per cent.)

In the pulse height method for determining  $\Delta E_p$ , the pulse height of those protons which stop in a crystal (or a proportional counter) is a measure of the energy (or range) of the protons that have penetrated the rest of the telescope. Guernsey *et al.* (32) employ a multi-channel differential pulse height analyzer to measure several groups of protons simultaneously. The error in  $\Delta E_p$  arises from the range straggling and the energy resolution of their detector. The energy resolution of their crystals is about 10 per cent [Mott *et al.* (60)].

In both methods, the actual value of  $\Delta E_p$  has to be corrected for the spread in energy due to the difference in the energy lost by protons produced at the back and front of the hydrogenous target.

In the laboratory system  $E_p$  is a function of  $\theta$ [q.v., Fig. 4 of Mott *et al.* (60), or the footnote in Hadley *et al.* (33)]. Therefore,  $\Delta E_p$  and  $\Delta\omega$  in the laboratory system are interrelated.<sup>4</sup>

$F(E_p)$ .—This factor is less than one because protons are lost in traversing the detecting system by Coulomb scattering, nuclear scattering, and nuclear absorption in the absorbers and detectors of the telescope. These losses increase rapidly above 100 Mev, and for 200 Mev protons  $F(E_p)$  will be of the order of 0.7.

<sup>3</sup> There may be some readers of this chapter who are unhappy with the use of the terms "uncertainty" or "error" in place of "standard error" or "probable error." The author of this chapter is restricting the use of the term "standard error" to those cases where the error arises from a known statistical fluctuation. The uncertainty of 3 per cent in  $\Delta\omega$  is an estimate by Chamberlain *et al.* and it is not a statistical fluctuation.

<sup>4</sup> In the required relativistic transformations between the center of mass and laboratory systems, the author has found it useful to employ the relativistic invariance of  $P\Delta E\Delta\omega$ , where  $P$  is the momentum.

The loss attributable to Coulomb scattering can be estimated with some assurance, or it can be measured [q.v., Hadley *et al.* (33) and Bodansky & Ramsey (16)]. The Coulomb scattering correction is very dependent upon the geometry of the telescope and can become appreciable if the absorbers are not close to the last detector in the telescope.

The loss attributable to the nuclear interactions of the protons is extremely difficult to measure. Such losses can be only crudely estimated, because the data on the nuclear absorption of high energy protons are still sparse [Bernardini, Booth & Lindenbaum (11)]. Working with 100 Mev neutrons, Bodansky & Ramsey estimated 5 per cent of the protons were lost due to nuclear effects. For 350 Mev neutrons Goodell *et al.* estimated 30 per cent of the protons were not counted in their telescope. The uncertainty in these estimates is very large.

From consideration of all of the above factors it can be seen that the most important factors leading to an uncertainty in an absolute measurement of neutron flux depend upon the energy of the neutrons. For neutrons with energies less than 150 Mev, the greatest uncertainty should be that arising from uncertainty in  $d\sigma/d\omega$ . For neutrons above 300 Mev, the largest uncertainty should be that in  $F(E_p)$  attributable to nuclear absorption.

#### RELATIVE MEASUREMENTS ABOVE 15 MEV

*Energy distributions.*—Knox (52) has shown that neutrons from synchrocyclotrons have a broad spread in energy due to multiple traverses of the cyclotron target by the proton beam. Due to this broad spread, nearly all the problems that arise in absolute measurements at these energies are present in determining energy distributions. Therefore no separate discussion will be given here of measurements of energy distributions. The most precise energy distribution measurements seem to be those of Cassels *et al.* (20) and Nelson, Guernsey & Mott (62).

*Relative intensity measurements.*—Attenuation measurements are not subject to the uncertainties that are discussed above since the factors of expression 1 all remain constant except for the changes in  $\phi(E_N)$  which are being investigated. In this case the experimental error essentially arises from the counting statistics. The proton recoil detectors are poor in the sense that they have very low overall efficiencies (when solid angle and hydrogen target thickness are included), namely,  $10^{-4}$  to  $10^{-5}$ . Simpler neutron detectors that have the same or higher efficiencies are therefore quite desirable. For these high energy neutrons, the Berkeley people have developed two other detectors. Kelly & Wiegand (50) and Wiegand (81) describe a bismuth fission chamber, and McMillan & York (58) have studied the  $C(n, 2n)$  reaction. This latter reaction leads to a 20 min. half-life positron emitter which is very convenient for counting. Cook *et al.* (23) and Bratenahl *et al.* (17) have used  $C(n, 2n)$  detectors. DeJuren & Knable (25) have employed the bismuth fission detector.

The efficiency of these detectors for various energy neutrons is discussed in the above mentioned references and is based on a comparison with a proton recoil detector [see McMillan & York (58)].

The present state of the knowledge of the energy dependence of the cross section for the  $C(n, 2n)$  and the fission of bismuth is limited. Consequently measurements made with these detectors are at an "effective neutron energy" whose uncertainty depends upon the energy spread in the initial beam of neutrons. However, as most phenomena at high energies are generally slowly varying functions of energy, such detectors have much to offer in the relative simplicity of equipment.

#### ABSOLUTE MEASUREMENTS FROM 0.01 TO 15 MEV

Neutrons in this energy region have been investigated for many years. A variety of methods have been developed for making absolute measurements. Description of these methods will be found in two very useful recent reviews, namely Barschall *et al.*, hereafter BRTW (8), and sections IIIC and IIIE of Feld (26).

The best methods for making absolute measurements with monoergic sources of neutrons appear to be the associated particle method and the recoil proton counter technique which are discussed below. Standard neutron sources up to the present have not been monoergic. The methods employed for calibrating such sources therefore require separate treatment.

*The associated charged particle method.*—In the neutron producing reactions



a reasonably energetic charged particle is emitted with every neutron. In principle, by measuring the associated charged particle one can determine the number of neutrons. This has been applied to the D-D and to the D-T reactions, [BRTW (8)]. In practice, one measures the charged particles emitted within a certain solid angle. As it is not convenient to be limited to exactly the corresponding solid angles for the neutron, one needs a knowledge of the differential cross section for the reaction [Blair *et al.* (15)].

Barschall *et al.* (8) state:

With presently available reactions and techniques it seems quite possible to make direct flux measurements to about one per cent in the energy range above 3 Mev using the DD reaction and above 13 Mev using the TD reaction. Such accuracy, however, has not yet been attained primarily because no serious attempts at the problem have been made.

The D-D, D-T and p-T reactions all require charged particle accelerators and therefore a measurement of the associated particles every time they are used. The photodisintegration of the deuteron,  $\gamma$ -D reaction, can be produced without the use of charged particle accelerators. However, the

neutrons from the  $\gamma$ -D reaction will have a fixed energy whereas the energy of those produced by a charge particle accelerator can be varied.

The cross section for the photodisintegration of the deuteron by the  $\gamma$ -rays emitted by a RdTh source is now known to about 4 per cent [Bishop *et al.* (14)]. However, a neutron source can be constructed the value of whose strength need not contain the uncertainty in this cross section. Halban (35) suggests that one measures the number of photoprotons (identical with the number of photoneutrons) produced in an ionization chamber filled with  $D_2$  by a RdTh source which is inserted into the chamber. If  $D_2O$  is substituted for  $D_2$ , the number of neutrons emitted is obtainable from the ratio of the number of D atoms present in the two fillings. There will be corrections of a fraction of one per cent. Halban believes that by this method it is possible to obtain neutron sources whose strengths will be known to the order of one per cent.

*The recoil proton counter technique.*—In this energy region the best known cross section is that of the scattering of neutrons by protons. [See Hafner *et al.* (34)]. It has been found that if one tries to make an absolute measurement by a recoil proton detector that the limitation in accuracy arises from knowledge of the response of the detector. The problems encountered in using detectors that measure individual pulses or the total ionization are discussed by BRTW (8) and Wilkinson (83). The relative merits of four types of recoil proton detectors for neutrons above 1 Mev can be found in the work of Allen, Livesey & Wilkinson (3). They compared the value of the flux determined by a homogeneous ionization chamber, a triple coincidence counter telescope, a gas-filled pulse ion chamber, and a thick radiator chamber. The four flux determinations showed a maximum variation of 6 per cent.

During the last year Skyrme, Tunnicliffe & Ward (75) have reported the development of a proportional counter for neutron flux measurements in the energy range 0.1 to 1 Mev. They state that absolute flux measurements can be made to better than 5 per cent and perhaps as well as 2 per cent. One of the main difficulties with counters as flux measuring devices is the uncertainty in the active volume of the counter which is due to wall and end effects. A proportional counter filled with hydrogen or methane has a continuous distribution of recoil proton energies. The shape of the pulse height distribution needs to be calculable in order to evaluate what fraction of the neutrons are being counted above some arbitrary bias. These authors calculated the expected pulse height distribution taking into account wall and end effects. They devoted great care to the design of the counter in order to make the end effects calculable. The result is that they find good agreement between the calculated and observed pulse height distribution, which indicates that they know the active volume of their counters.

An application of their technique to an accuracy of 2 per cent would require a knowledge of the amount of hydrogen adsorbed on the walls as a function of time, the attenuation of the neutrons by those parts of the counter through which the neutrons pass, and the variation about the



mean of the ionization loss (not energy) of protons in methane or hydrogen. Even the 5 per cent accuracy they have achieved makes the effort in construction of such detectors very worthwhile. Such detectors are very appealing from the point of view of the ease of measurement of fast neutron flux.

*The calibration of standard neutron sources.*—Neutron research centers have found it convenient to possess a calibrated neutron source. Such a source is useful in determining the efficiencies of neutron detectors and the number of neutrons emitted by other neutron sources. The majority of these standard sources at present are intimate mixtures of a radium salt and beryllium metal making use of the  $(\alpha, n)$  reaction on  $\text{Be}^9$  [q.v., Anderson & Feld (6)]. Other neutron sources have been proposed which would have the desirable property that the neutron emission would be directly proportional to the amount of radioactive material and would be stable over long periods of time. The  $\text{RdTh}$  plus  $\text{D}_2\text{O}$  source of Halban (associated charged particle method) would have this property. Bretscher *et al.* (82) have investigated a source which is a fixed chemical compound, namely  $\text{RaBeF}_4$ ; Curtiss and associates at the U.S. National Bureau of Standards have been studying a radium-beryllium photoneutron source, that is, one making use of the  $(\gamma, n)$  reaction in  $\text{Be}^9$  with the radium in a separate container [Carson & Curtiss (19)]. No recent developments have been reported on either of the last two sources.

The techniques described above for calibrating monoergic sources are not useful in calibrating the existing standard sources due to the continuous distribution of energies of the neutrons emitted by beryllium sources. Methods which integrate over the entire spectrum are necessary. The oldest such method is frequently referred to as the water bath method, even though any hydrogenous material may be employed. In this technique all the neutrons are brought down to low energies by collisions with hydrogen. Then a space integration of some "fraction" of these neutrons is performed with a  $1/v$  or resonance neutron detector. Almost every person who has applied the technique has introduced some new variation. The determination of the neutron source strength becomes a matter of evaluating this "fraction." Generally, this requires a determination of the ratio of the capture cross section in hydrogen to the capture cross section of the detector and the absolute efficiency of the detector. (A discussion of the absolute efficiency of low energy neutron detectors is given in another section.) Alvarez proposed a method in which the "fraction" becomes essentially unity; the determination of the absolute efficiency of the detector in his method becomes the accurate measurement of a small quantity of helium [Seidl & Harris (72)]. Feld, [(26), Sec. IIIE], gives a nice concise explanation of the basic principles underlying the majority of the variations of the water bath technique. Recent applications of the technique have been made by Alder & Huber (2), Bracci, Facchini, & Germagnoli (18), O'Neal & Scharff-Goldhaber (64), and Walker (79). The latter is the most detailed. The water bath technique has been applied to measuring the number of neutrons from a charged particle accelerator by Taschek & Hemmendinger (77).



Up to the present time the majority of workers using the water bath technique have obtained values with an uncertainty of about 5 per cent. The recent developments in measuring absolute disintegration rates and the effort being devoted to measuring slow neutron reactions cross sections (q. v. "Absolute Measurements at Low Energies") appear to make it feasible to reduce the uncertainty to 3 per cent in future applications of the water bath method.

Littler (54) has developed a very clever method of calibrating neutron sources which makes use of a chain reacting pile, a nuclear reactor. A naive understanding of the basis of the technique can be obtained from the following considerations. If a source of neutrons is introduced into a nuclear reactor, the pile power will rise or, effectively, the reactivity of the pile will increase. If, instead of a source, one introduces a sink or absorber of neutrons, the pile reactivity will decrease. If the number of neutrons absorbed in the sink per second is the same as the number of neutrons emitted by the source, then neglecting the energy of the neutrons to a first approximation, one would obtain equal and opposite effects. If an element with only one stable isotope is used as the sink, then the rate of absorption of neutrons is equal to the saturated disintegration rate of the radioactivity produced. The measurement of the strength of a neutron source thus becomes the determination of the disintegration rate of a radioactive sample.

An equal and opposite effect is not necessary as the effects are small and therefore linear to a sufficient accuracy. Actually, the source is oscillated in and out of the pile to obtain a higher accuracy on the measurement of the perturbation of the pile power. The source contains material which absorbs neutrons and a correction for the absorption is necessary.

There is also a correction for the fact that the neutrons from the source are at high energies and the sink is absorbing mainly thermal neutrons. For the accuracy to which the method has been applied, the uncertainties in the energy-correction factor are not important. One of the great values of this technique lies in the fact that this correction factor varies very little with the energy of the neutrons emitted by a source.

The absolute determination of the disintegration rate was obtained on  $\text{Na}^{24}$  by the coincidence technique (discussed in the section on "Absolute Measurements at Low Energies" below). A minor correction to the original paper of Littler (54) is described in the report of Littler *et al.* (55). The error quoted for their result is  $4\frac{1}{2}$  per cent in an absolute calibration. The pile method appears not only to have the advantage of requiring relatively fewer measurements but also of having given the greatest accuracy as of the present time.

A check on the reliability of all of the techniques discussed above is provided by a series of intercalibrations of standard neutron sources. The data given below under the heading of "The current status of the intercalibration of standard neutron sources" indicate that the majority of absolute measurements made to date are well within their stated errors.

## RELATIVE MEASUREMENTS FROM 0.01 TO 15 MeV

*Energy distributions.*—The development of photographic nuclear emulsions has led to progress in determining neutron energy distributions at energies above 0.5 Mev. Neutrons which scatter off the hydrogen in a nuclear emulsion produce recoil proton tracks. There is an appreciable literature in this field already which will be found in Feld, [IIC4 (26)]. However, the successful use of this technique requires the good geometry employed by Preston & Stelson (76), Houtermans & Teucher (39) and the Wisconsin group, namely, Ajzenberg (1, 69), Johnson, Laubenstein & Richards (46, 69). (The first two give references to their other work.) The Wisconsin group have limited themselves to those recoil protons in the forward direction that make an angle of less than  $15^\circ$  with the direction of the neutron and have less than a  $3^\circ$  dip into the emulsion (46). They have used neutrons to obtain an energy calibration of their plates. Ajzenberg (1) was able to obtain the angular distribution of seven energy groups of neutrons between 0.5 Mev and 8 Mev in the reaction  $\text{Be}^9(d, n)\text{B}^{10}$ . In this work, Ajzenberg found a resolution of 100 kev for 2 Mev neutrons and a resolution of 300 kev for 8 Mev neutrons.

In applying the photographic emulsion technique it is worthwhile to take elaborate precautions against scattered neutrons [Preston & Stelson (76)]. Even a background of thermal neutrons produces proton tracks by the  $\text{N}^{14}(n, p)\text{C}^{14}$  reaction with the nitrogen present in the emulsion. There are difficulties in using the photographic technique for obtaining absolute values. One of the more serious ones is that the amount of hydrogen in the emulsion depends upon the humidity, [Barschall *et al.* (8)].

Due to the recoil proton tracks becoming very short, the emulsion technique is not very valuable below 0.5 Mev. However, at lower energies essentially the same principles can be applied by substituting a hydrogen-filled cloud chamber for the nuclear emulsion. Hughes & Eggler have successfully measured neutron energy distributions in the region from 0.02 to 1.0 Mev (42).

An interesting proportional counter that promises to be useful in determining neutron energy distributions up to 1 Mev has been developed by Batchelor (9). His counter contains  $\text{He}^3$  and makes use of the exothermic reaction  $\text{He}^3 + n \rightarrow \text{H}^1 + \text{H}^3 + 770 \text{ kev}$ . The reaction products are both charged. Therefore, the pulse height is directly proportional to the neutron energy and is independent of angles. He gives references for the value of the cross section as a function of energy. The pulses from a 560 kev monoenergetic neutron source have a 150 kev width in his present detector, and the pulses from thermal neutrons have a 55 kev width. The method is limited to energies below 1 Mev because  $\text{He}^3$  recoils from neutron scattering become confused with the main peak. The maximum  $\text{He}^3$  recoil from a 1 Mev neutron is 0.75 Mev.

Two neutron spectrometers have been described in the last year which select only recoil protons in the forward direction. Nereson & Darden (63)

have built an extremely elaborate proton recoil ionization chamber. In this chamber they measure only those recoil protons that pass through a collimator with a  $10^\circ$  cone. Their detector has been used in the 3 to 12 Mev range. Beghian *et al.* (10) use two scintillation counters and a very fast coincidence circuit with a time delay. They select forward recoil protons by requiring that the neutron after producing the recoil proton be left with less than 30 kev as determined by time of flight.

In both these neutron spectrometers the pulse height distributions obtained from monoenergetic neutron sources show low-energy tails.

*Relative intensity measurements: measurements with monoenergetic sources.*—The majority of the techniques developed for relative measurements have been employed in determining cross sections. The techniques for such measurements are described by Barschall (7). I shall therefore limit myself to listing the sources of error encountered in four measurements reported during the last year where accuracies of about three tenths of one per cent have been obtained. Frisch & Storrs (29) made measurements with about 1.310 Mev neutrons; Fields, Becker & Adair (27) worked with  $2.532 \pm 0.006$  Mev neutrons; Hafner *et al.* (34) worked with  $4.749 \pm 0.009$  Mev neutrons; Poss *et al.* (66) worked with  $14.10 \pm 0.05$  Mev neutrons. Frisch & Storrs, by using a propane filled proportional counter were able to discriminate against lower energy background neutrons. However, they found that the discrimination is affected by the counting rate. To avoid such corrections they varied the source strength to compensate for the insertion of a scatterer, thus obtaining the same counting rate in their detector. The source strength was monitored by means of a "long counter" (see below). Frisch & Storrs also kept a constant check on the energy of the neutrons by running with their average energy held at a neutron-scattering resonance in oxygen. Fields, Becker & Adair studied the energy distribution of their neutrons by a beautiful technique employing a narrow resonance in carbon.

Hafner *et al.* used scintillation neutron counters described by Hornyak (38). Each counter fed two independent discriminators and scalers, operating at different counting rates, as a check on scaler pile-up, dead time effects, and drift of bias. Runs were made at high and low neutron flux as an additional check of counting rate dependence. In an appendix they calculate the effect of the pile-up of pulses. Hafner *et al.* give a more detailed discussion than appears elsewhere of the many considerations involved in such precise measurements. Among the points discussed are: geometry, energy spread of the neutrons,  $\gamma$ -ray background, counting rate effects, background neutrons scattered into the detector by the surroundings, the number of atoms in a scatterer, the energy of the neutrons and spurious neutron backgrounds. They evaluate twelve sources of error in determining cross sections by attenuation; seven of these are of the order of one tenth of one per cent.

Poss *et al.* used a liquid scintillation counter with a 5 per cent efficiency. They monitored by observing the helium ions from the D-T reaction which they were using as a source of neutrons. They describe more briefly the checks

they made on many of the sources of errors listed in the paper of Hafner *et al.* (34). They encountered a small background of three tenths of one per cent due to cosmic ray events. Their paper contains two appendices: one concerned with the energy spectrum of the neutrons, and the other with the "scattering-in" of neutrons by an attenuation sample. The latter takes into account the diffraction of neutrons.

*Measurements with neutrons from  $\alpha$ -ray and  $\gamma$ -ray emitters.*—If one desires a quick method of comparing neutron source strengths, the "long counter" is the most useful tool. A "long counter" is a standardized cylinder of paraffin with a  $\text{BF}_3$  cylindrical detector along its axis [Hanson & McKibben (37)]. The reliability of a comparison of two sources with different energy spectra has been limited by the uncertainty in the efficiency of a "long counter" as a function of energy. The new calculations of Kushneriuk (53) should help a great deal in reducing the uncertainty due to the energy dependence. The efficiency of the long counter as a function of energy is calculated by Kushneriuk using a two-group model of neutron diffusion in conjunction with the age and exponential approximations for the slowing down of neutrons. Neutron energies considered are less than 10 Mev. His results are summarized graphically for several counter geometries and vary from efficiencies of  $4 \times 10^{-3}$  to  $1 \times 10^{-3}$ . For the geometry employed by Hanson & McKibben which was found to have an efficiency of about  $4 \times 10^{-3}$ , he calculates that the efficiency should be  $3.9 \times 10^{-3}$ .

Because of the flatness of the response of this detector as a function of neutron energy, the long counter appears to be limited by counting statistics only in comparing the source strength of two neutron sources of approximately identical energy distributions. However, those who have employed such counters have encountered other sources of error. The most frequently overlooked error is that the emission from a macroscopic source is not isotropic. Littler *et al.* (55) find that with an Anderson-Feld type source (6) the emission from the end without a protuberance is  $0.901 \pm 0.014$  of the emission from the end with a protuberance. Wattenberg & Eggler (80) observed that the majority of cylindrically shaped neutron sources have a slightly greater emission of neutrons radially than along the axis of the cylinder. For accurate measurements, one must also determine: the natural background of cosmic ray events, the number of neutrons being scattered by the surroundings, and the counting rate dependence of the detector and electronics. One must also investigate the effects, if any, of the background of  $\gamma$ -rays emitted by all such sources of neutrons. Such  $\gamma$ -rays may not give pulses by themselves, and yet the number of  $\gamma$ -rays may change the apparent neutron counting rate if the  $\text{BF}_3$  detector does not have a perfectly flat plateau.

After making corrections for the above consideration the latter authors have found that the ratio they obtained for the strengths of two RaBe neutron sources agreed to about 1 per cent with the ratio obtained by other techniques.

The water bath techniques described above in the section on absolute measurements are frequently used to compare sources. If the sources are not identical in shape as well as spectrum a space integration is necessary. Obviously for the comparison of two sources, the absolute value measurements in these techniques are not necessary. A graphite geometry is basically similar to a water bath, but it is less critical as to sizes of source, position from source, temperature, as well as being mechanically more stable [q.v., Hughes (41, pp. 77, 81); appendix to Walker (79)].

Two methods which employ a nuclear reactor or pile have been found very convenient for comparing the strengths of neutron sources. Both methods make use of the property of piles that the effect on the pile of introducing a source is almost completely independent of the energy of the neutrons from the source and the variations in the spatial emission. The two pile methods are quite different. The method of Littler (54) has already been described above in the section on absolute measurements. For relative measurements by Littler's method, essentially all that has to be done is to compare the effect on the pile of two different sources and to correct each effect for the neutron absorbing materials present in each source.

The other method that employs a pile is that of Wattenberg & Egger (80). Their method depends upon the fact that a sub-critical pile multiplies the number of neutrons emitted by a source placed inside of it. Thus, if one places a neutron detector in a fixed position at the surface of a pile, its counting rate will vary directly as the strength of a neutron source placed inside the pile in a fixed position. There is a background of neutrons always present even in a sub-critical pile which must be subtracted from the counting rate.

The difference in the techniques is fundamentally that in the sub-critical pile method the neutron flux in the pile is mainly due to the neutron source, whereas in Littler's method the effect of the source is a perturbation on the neutron flux. However, extremely small perturbations of pile reactivity can be measured accurately; therefore, there is comparatively little advantage of the one technique over the other for comparing two sources. The most important difference is that Littler's technique permits of an absolute calibration, and the sub-critical pile method does not.

The advantage of both techniques over all others occurs in the comparison of two sources with different energies. If a pile technique is used, then the correction for the difference in the energy of the sources is normally of the order of tenths of a per cent and can be calculated accurately. An extreme correction of about 2 per cent is needed if one of the sources emits 0.030 Mev neutrons and the other source emits 2.0 Mev neutrons.

Littler has employed his technique with sources that emit  $10^6$  to  $10^7$  neutrons per second. The sub-critical pile technique has been employed on sources that emit from  $10^5$  to  $10^7$  neutrons per second. Both techniques have yielded ratios with an uncertainty of one per cent. If greater accuracy in ratios is ever needed, further study of these techniques will be required.



*The current status of the intercalibration of standard neutron sources.*—Littler & Lockett (56) using the sub-critical pile technique made a comparison of independently calibrated standard sources from Sweden and America (Los Alamos source #40) with the independently calibrated 1290 mg. source of Harwell, England. The ratios obtained by Littler & Lockett indicated agreement of the Swedish-British calibration to about 3 per cent and the Los Alamos-British calibration to 1 per cent. This is amazing agreement as the best of the independent calibrations have quoted errors of over 4 per cent. Hughes [(41) pg. 76] compared two independently calibrated American sources, namely #38 of the Argonne National Laboratory [Seidl & Harris (72)] and #44 of the Los Alamos Laboratory [Walker (79)]. He found that the Argonne value is 5 per cent higher than the Los Alamos value; however, the quoted errors on these source strengths are 7 per cent and 5 per cent respectively. Comparisons have also been made of a Canadian standard source and the American source #38 from the Argonne [Almqvist (5)]. Comparisons also exist between Italy and Basel (Switzerland), Italy and France, Basel and Sweden, and Basel and Harwell, [Huber (40)]. Unfortunately, there is a 20 per cent discrepancy in this chain of intercomparisons. However, the situation is not clear as reports on some of the comparisons are not yet published.

The excellent agreement of the independent calibrations of England, America, and Sweden is considered to have decreased the uncertainty in the absolute value of the 1290 mg. source at Harwell to about 3 per cent [Littler & Lockett (56)]. The state of our knowledge of neutron source strengths is definitely improving.

#### ABSOLUTE MEASUREMENTS OF LOW-ENERGY NEUTRONS

An absolute flux or density of low energy neutrons can be measured by many techniques. The two techniques in which advances have been made recently are the photographic plate technique and the activation method.

*The photographic plate technique.*—Although the accuracy achieved up to the present with the photographic plate technique does not compare favorably with the precision of other methods, it is a valuable development in that it extends the range of flux measurements. Kaplan & Yagoda (48), by loading plates with lithium borate, have been able to measure neutron fluxes as low as  $2 \times 10^{-3}$  neutrons per square centimeter per second. In order to avoid the accumulation of cosmic ray neutron tracks in their emulsion, they perform the loading themselves. All the details are given in their paper for the preparation and standardizing of such emulsions. By using lithium borate and counting the tracks produced by the  $\text{Li}^6(n, \alpha)\text{H}^3$  reaction and the  $\text{B}^{10}(n, \alpha)\text{Li}^7$  reactions separately, they obtain a relative internal check. The method appears capable of yielding results with a standard error of 10 per cent, if the order of 500 or more tracks are counted.

*The activation method.*—The majority of recent absolute measurements have been obtained with neutrons which are in thermal equilibrium with



diffusing media so that the neutrons have a Maxwell-Boltzman distribution of velocities. Neutron flux or density measurements are made both in diffusing media and with well collimated beams.

The activation techniques are based upon the relationship that the activity (absolute disintegration rate) in an infinitely thin sample is given by

$$A = (1 - e^{-t/\tau}) \int_0^\infty n v N \sigma_a dv \quad 2.$$

Where  $A$  is the activity in disintegrations per second at the end of an irradiation,  $n$  is the density of neutrons (which density is a properly normalized Maxwell-Boltzmann distribution of velocity),  $N$  is the total number of atoms in the sample having a cross section  $\sigma_a$  for producing the activity with mean life  $\tau$ , and  $t$  is the length of time the sample is irradiated.

Generally an element is employed with a  $1/v$  activation cross section, i.e.,  $\sigma_a = \sigma_0/v$  where  $\sigma_0$  is a constant. Then

$$A = (1 - e^{-t/\tau}) N \sigma_0 \int_0^\infty n dv \quad 3.$$

As  $\int n dv$  is the total density of neutrons and is independent of the temperature of the neutrons, expression (3) is the basis for talking about a measurement of a density of neutrons.

In order to determine a neutron flux or density  $\tau$ ,  $\sigma_a$ ,  $N$ , and  $A$  must be known in advance or determined. The two quantities that are most difficult to determine are the activation cross section,  $\sigma_a$ , and the absolute disintegration rate,  $A$ . The recent developments in determining absolute disintegration rates are therefore of great importance in improving the accuracy of neutron flux measurements. The effort involved in reducing the error in  $A$  to a few per cent is very great as brought out in the paper of Cohen (22). He uses manganese as a neutron detector. Because  $\text{Mn}^{56}$  has a complex  $\beta$ -decay scheme, Cohen devoted his efforts to the development of a " $4\pi$ " counter. By checking it with a  $\text{Na}^{24}$  source, he found it to be 100 per cent efficient. (He established the absolute disintegration rate of the  $\text{Na}^{24}$  source by coincidence counting.) Cohen's paper contains an excellent discussion of many of the sources of error in absolute  $\beta$ -counting and why he personally chose a " $4\pi$ " counter. After rather elaborate investigations Cohen felt he had obtained the absolute activity of  $\text{Mn}^{56}$  to 2 per cent.

Katcoff (49) measured an absolute flux by activating gold. He determined the activity by the  $\beta$ - $\gamma$ -coincidence technique. In determining the absolute disintegration rate of gold, he had to correct for the 4 per cent of the  $\gamma$ -rays which are internally converted. It is unfortunate that his discussion of the flux measurement is so brief. He checked a gold foil against an aliquot from a gold solution, and the values of the flux so obtained agreed to 4 per cent.

Little, Lockett & Price (57) obtained an absolute calibration of the flux in the Harwell piles using the  $\beta$ - $\gamma$ -coincidence counting of  $\text{Na}^{24}$ . It was checked against a measurement of the flux with  $\text{Mn}^{56}$ , [Price (67)]. The abso-

lute counting of the  $\text{Mn}^{56}$  was performed by the defined solid angle technique. The two measurements of  $A$  agreed to 2 per cent.

The care taken in making absolute disintegration rate measurements at Harwell by the coincidence method, the defined solid angle method, and the " $4\pi$ " counter method, is described by Putnam (68). Putnam has done a great service for others in pointing out the errors that can arise from the approximations usually made in applying the  $\beta$ - $\gamma$ -coincidence technique. It is a pleasure to see finally in the literature that the counting rates are really volume integrals over the sample of the efficiencies of counting. Consequently, the ratio one obtains has a denominator with an integral of a product and a numerator with a product of integrals. Unfortunately, he did not extend these expressions to the case where internal conversion electrons are present. However, he does point out that the electron counting efficiency may be different than the efficiency for counting  $\beta$ -rays. He is careful to use substances with a negligible internal conversion coefficient in determining absolute disintegration rates by the coincidence counting technique. Putnam also points out the need for: auxiliary quenching of the counters, accurately determining dead time losses, correcting for the accidental coincidence rate, and correcting for background coincidences. Putnam's article would have been almost perfect if it had also contained some discussion of the loss of coincidence counts due to the fluctuation of delay time in detectors. This loss can be of the order of several per cent if the resolving time of the coincidence circuit is appreciably less than 1 microsecond. The standard error of Putnam's coincidence measurements is 1.2 per cent due to the counting statistics.

In expression 3 the other main source of uncertainty is  $\sigma_a$ . It will be seen from the recently published compilation of neutron cross sections sponsored by the U. S. Atomic Energy Commission (44) that not many activation cross sections are known to even 5 per cent.

Cohen (22) has not yet published the basis for using an activation cross section of manganese of 13.2 barns so no analysis of the error arising from  $\sigma_a$  can be made here. His value is in agreement with the cross section quoted in the compilation (44) of  $12.6 \pm 0.6$  barns. Katcoff (49) used a cross section of 95 barns for the activation cross section of gold. The value given in the compilation for the activation cross section of gold is  $94 \pm 1$  barns. Gold, unfortunately, is not exactly a  $1/v$  absorber because of a neutron absorption resonance at 4.8 ev. The deviation from the  $1/v$  is only the order of one-half per cent in the thermal region; however, the resonance requires that corrections be made for the activation of the gold by the resonance neutrons. The correction for resonance neutrons is usually determined by activating the sample with and without a cadmium covering. Such a procedure requires corrections of the order of 20 per cent for the effect of the cadmium, [Hughes (41) pg. 88].

Littler, Lockett & Price (57) used sodium and compared its activation cross section with that of boron. As many workers use boron as a standard,

they are in the position of being able to adjust the value of their flux to any improved measurements of the cross section of boron. The present uncertainty in the cross section of boron is about 1.5 per cent.

Several possible sources of error in absolute flux or density measurements deserve discussion. Expression 2 and expression 3 assume the samples being activated are infinitely thin. This is never the case. Actually, even in the measurements made in neutron beams, the samples attenuate the neutron flux within themselves. This attenuation is a function of the velocity of the neutrons. For the case of a collimated beam, the correction for the attenuation can be estimated readily for thin samples. The correction is a little less than the amount by which the sample attenuates the beam. If the sample attenuates the neutrons by less than 1 per cent, the correction to the determination of the flux will also be less than 1 per cent and not very serious.

However, inside diffusing media the correction for the thickness of the sample is larger as the flux is depressed in the neighborhood of the sample. Klema & Ritchie (51) found experimentally that a correction is needed that is approximately five times the attenuation of a perpendicular beam of neutrons in the sample. Therefore, unless a sample is used which has an extremely small attenuation one will have to investigate such corrections. The same consideration of the attenuation needs to be applied to neutron counters used in measuring flux.

If accuracies of the order of a few per cent are desired, it may be necessary to look into the effect of deviations from the Maxwellian distribution. It is already known that at the Bragg limit in polycrystalline media deviations from a Maxwellian distribution occur.

The present status of published absolute neutron flux or density determinations can probably best be judged from the careful work of Littler, Lockett & Price (57) who give 5 per cent as the overall uncertainty in their value of the flux.

#### RELATIVE MEASUREMENTS FOR LOW-ENERGY NEUTRONS

*Relative energy measurements.*—At low energies quite a few techniques are available for either producing beams of neutrons at a known energy or selectivity counting neutrons in a narrow velocity group. The former techniques include crystal spectrometers, polycrystalline filters, neutron mirrors, and mechanical monochromators. The counting of neutrons with selected velocities is performed by the use of a mechanical chopper or a pulsed particle accelerator and time-of-flight equipment or by the nuclear resonance scattering of neutrons. All these techniques are excellently described by Hughes (41). A description of such techniques and their limitations would require one or more volumes. Constant improvements in technique and apparatus now have made possible the specification of neutron energies to an accuracy of three figures.

However, it is a much more difficult task to determine the number of neutrons emitted at different energies. The number of neutrons at different

energies reflected by a crystal spectrometer is an important quantity in some experiments. It depends upon the form factor, the imperfections in the crystal, the original distribution of the neutrons hitting the crystal, etc. These questions will be discussed in a book to be published by Shull & Wollan (74). The energy distribution from velocity selectors and mechanical monochromators varies very much with the design, the acceptable neutron paths as a function of operation parameters, the geometry of the detection equipment, the energy dependence of the initial source of neutrons, etc. For the measurements normally made by these devices, the understanding of the number of neutrons as a function of energy is fortunately only of interest in estimating corrections and energy resolution.

It is not a simple matter to obtain the actual distribution in energy of a source of neutrons. When one has neutrons in diffusing media, a Maxwell-Boltzmann distribution is assumed, and it is convenient to talk in terms of the temperature of the distribution. The most common method of obtaining the temperature is by a transmission measurement on a  $1/v$  absorber with a known cross section. Therefore, one uncertainty in the temperature arises from the error in the value of the cross section. If one uses a " $1/v$  detector" the effect of the change in the energy distribution due to the finite attenuation in the absorbing sample can be obtained from the curve in Bethe (13) or, more exactly, from the expressions given by Zahn (84). Zahn also gives the expression for the transmission of a  $1/v$  absorber measured by a black detector, i.e., one that has 100 per cent efficiency for detecting neutrons. It is important that the detectors be  $1/v$  or black. In work at the Argonne National Laboratory, Jankowski & Wattenberg (45) found that when they used a detector that had a 95 per cent efficiency they obtained a value of the temperature that was 15 per cent higher than the value obtained with a detector that had a 99.7 per cent efficiency (for the mean energy neutrons). No similar studies on so called " $1/v$  detectors" have come to the attention of the author of this article. These uncertainties and others discussed by Hughes [(41), pg. 91] may possibly account for the variations of 20 per cent in the value of the temperature obtained by different groups.

*Relative intensity measurements.*—For standardizing detectors, the Atomic Energy Commission laboratories have found it convenient to have a pure graphite geometry with a standard neutron source in it permanently. The distribution of neutron flux as a function of position in such a graphite pile remains unchanged in time. The absolute value of the flux is known to the accuracy of the source strength, namely 5 to 7 per cent [q.v., pg. 80 of Hughes (41)].

Klema & Ritchie (51) showed that the detectors one is studying may seriously perturb the flux distribution. Therefore, such an arrangement is useful for accurately comparing detectors only if one knows the ratio of the perturbations of the flux caused by the detectors. However, such graphite piles have proven very useful in checking the variation in detecting efficiency of foils which are supposed to be "identical." Generally, the limitation

on the determination of the relative response of "identical" detectors has arisen from the limited amount of activity that could be induced. This leads to a limited number of counts. In general, even the best comparisons have had uncertainties greater than one half of one per cent.

At Harwell, Littler, Lockett & Price (57) have calibrated an ion chamber in terms of the flux in Gleep. They are in a position to standardize neutron detectors in a flux that is known to 5 per cent. Again there is a correction required for the perturbation that occurs in the neighborhood of a detector.

Fairly precise relative measurements are readily made by activating foils. However, if one desires accuracies of 1 per cent or better, many complications enter the picture. The uniformity of the foils becomes important; the dead times of the counters must be determined; half-life values in the literature are frequently not sufficiently accurate to correct for the irradiation time or for the decays involved, and the effects on the detectors of higher energy groups of neutrons must be investigated. Such difficulties have limited the majority of measurements employing foils to having uncertainties greater than one half of one per cent in relative values.

Relative measurements reliable to the order of 0.1 per cent have been made with the aid of  $\text{BF}_3$  proportional counters and pulse ion chambers. Within the last year, two examples of such measurements will be found in the work of Hughes, Harvey & Goldberg (43) and Hamermesh, Ringo & Wattenberg (36). Both of these articles are too brief to be of much assistance to others. Many of the considerations discussed by Hafner *et al.* (34) also are involved in measurements at low energies. For such precise measurements, internal monitoring of the stability of the counting system and the source of neutrons is needed. In the first of the aforementioned articles, two beams of neutrons from a pile were used simultaneously. In the second reference five independent detectors and counting systems were in operation simultaneously. Another important point is that counting rate corrections should be avoided, if possible. One way to do this is described by Melkonian (59). He placed in a beam of neutrons a device which he called a "standard filter," to decrease the intensity of the beam. The transmission of the filter is arranged to be a purely geometrical matter. In determining the attenuation of a sample the "standard filter" is substituted for the sample. The thickness of the sample is such that the counting rates are essentially the same with the sample or with the "standard filter" in the beam. Thus, the counting rate corrections become negligible.

The more recent precise relative measurements of low-energy neutrons have been made possible to a great extent by the intense beams of neutrons now available.

#### SUMMARY

At the present time absolute measurements are only accurate to about 4 per cent for nearly all energy neutrons. The precision of relative measurements has been steadily but slowly coming into the region of a few tenths of



a per cent accuracy. The motivation for many of these improvements has come from a desire to measure more accurately the interaction of fundamental particles. In the future a quick check on what is achievable in relative neutron measurements can probably be obtained by looking up the most recent measurements of the neutron-proton interaction, the neutron-electron interaction, and the photodisintegration of the deuteron.

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# PHOTOGRAPHIC EMULSIONS<sup>1</sup>

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## INTRODUCTION

Because of its versatility, the detection of nuclear particles by photographic emulsions occupies an almost unique position among the various methods available for experimentation in nuclear physics. As in the cloud chamber, nuclear particles responsible for the tracks can be identified in a wide range of situations and their direction in space is readily determined. In addition, the photographic plate technique has a certain simplicity and, in its less refined forms, is inexpensive. The plates can be simply used as particle recorders, when it is sufficient to count the number of identical tracks occurring over a certain area. They are then in strong competition with more automatic detectors such as counters, but have the very definite advantage of easy discrimination, even, for instance, for detecting nuclear particles in a high background of electrons and  $\gamma$ -rays. This property makes them a first choice for exploratory experiments with particle accelerators of all energies. A number of measurements can be performed on the tracks themselves, and accordingly, provide the means of making the plate an increasingly refined instrument, adapted for instance to the detailed analysis of all tracks belonging to even extremely complicated nuclear events. In addition, combinations can be made of plates with other techniques, such as absorbers of various materials or deflection in a magnetic field, thus extending even further their field of usefulness. Other properties of plates may enhance their choice for experiments. Among these properties there are: small size and weight, ability to integrate events occurring over a long period of time, and relatively high density. The last property has the special advantage of quickly bringing to rest charged particles traversing them, enabling one sometimes to observe decay at rest of unstable particles ( $\mu$ ,  $\pi$ ,  $\tau$ ,  $\kappa$  mesons), etc. Disintegrations of the nuclei of the emulsion itself are often observed, but the interpretation of these experiments is made difficult by the chemical complexity of the emulsion.

Very useful introductions to the basic techniques are found in the book of Rossi (1), in an article of Fowler & Perkins (2) and, with much information on procedures and applications, in a review article by Rotblat (3). Another review giving a broad picture is that of Beiser (4). An interesting historical account is found in a recent article by Vigneron (5), while early stages of the technique were reviewed by Shapiro (6) and, in more restricted fields, by Demers (7). The reader will certainly find a reward in looking at the beautiful microphotographs of the book by Powell & Occhialini (8). Much information

<sup>1</sup> The survey of literature pertaining to this review was concluded in February, 1953.

on the use of emulsions for radioactive measurements, low-energy reactions, and applications to various fields, is found in a book by Yagoda (9). Many applications to the field of meson physics are reviewed by Powell (10).

The scope of the present chapter is limited. Only the measurements to be performed on the tracks themselves are examined. In addition it has been thought useful to include a discussion of processing techniques which are the basis of any successful experiment. The emphasis is mostly centered on the major progress of recent years, the use of more sensitive emulsions in great thicknesses, extending the application of the method to the high-energy region. But the author does not feel competent to do justice to what are perhaps the most fundamental aspects of the technique, those connected with the photographic process itself. No account is given, for instance, of the problems of emulsion manufacture for which the makers of emulsion have given the physicists indefatigable help. Yet the importance of research in the difficult fields of the mechanism of latent image formation, the factors affecting sensitivity, and the interpretation of development and fixing processes cannot be overemphasized. In their study may lie the key to radical improvement of the technique. The reader will probably find the best introduction to these questions in the very interesting review of Waller (11). Some of the material of this chapter of necessity parallels that of the reviews already quoted, although duplication is avoided when it is felt that the reader can be referred to them for a more complete treatment than space limitations would here allow. No mention is made, for instance, of the simplified processing methods which can be used in the lower energy region with thinner plates of less sensitivity (3, 4). The numerous precautions necessary to achieve good microscopic observations and measurements are not discussed (3, 12). Nor is there discussion of specific uses of the plates for the detection of neutral particles (3, 4), for applications to nuclear physics (3, 4, 8, 9), cosmic rays (13, 14), geology (11), etc.

The methods available today for the use of emulsions result from painstaking efforts of many workers. Significant improvements are often communicated from one laboratory to the others by way of visits or friendly letters. As a result, it is difficult to give always proper credit to authors by bibliographic references, which should be interpreted, when given in the present text, as guidance only to more detailed treatment.

#### PROPERTIES OF EMULSIONS

Emulsions sensitive to tracks of minimum ionization are manufactured in the United States by Eastman Kodak [type NTB 3 (15)], in England by Kodak [type NT 4 (16)], and by Ilford [type G 5 (17)]. Some authors have made their own emulsions (18, 19). As an illustration, Table I lists some of the properties of the Ilford G 5 emulsions. The reader will find data on a number of emulsions of different sensitivities, some of them loaded with specific elements, in the data sheets published by the manufacturers (15, 16, 17, 20) and in the review articles already quoted. It is of interest to note

that Ilford produces several types of "diluted G 5" emulsions, sensitive to minimum ionization, where the gelatin content has been increased, thus substantially augmenting the proportion of light elements (20, 21). Manufacturers are most helpful in supplying physicists with plates of almost all sizes and shapes upon request, although they have established convenient standard sizes. The thickness of the emulsion commonly used has much increased in recent years; Ilford reports (20) that 400, 600, 1000 and 1200 $\mu$  emulsion layers are produced regularly and that 2000 $\mu$  has occasionally been made. Also available are emulsions without glass backing, sometimes called "pellicules" or "stripped emulsions," which are very useful, as they can be stacked into a large sensitive volume. The relative position of the layers is usually ascertained by exposures to thin pencils of x-rays to facilitate the observation of the successive segments of tracks in each pellicule after processing. Ilford (22) also supplies emulsion in gel form and treated glass for special applications when it is essential that the experimenter pour his own plates to avoid any preliminary exposure.

TABLE I  
DATA ON ILFORD G 5 EMULSIONS\*

Composition†			
Density	3.907 gm./cm. <sup>3</sup>	Silver	1.85 gm./cm. <sup>3</sup>
Atoms/cm. <sup>3</sup>	$8.12 \times 10^{23}$	Bromine	1.36
Mean A	28.98	Iodine	0.024
Mean Z	13.17	Carbon	0.27
Mean Z <sup>3</sup>	456	Hydrogen	0.056
Radiation length	2.93 cm.	Oxygen	0.27
		Sulfur	0.010
		Nitrogen	0.067

\* In equilibrium with an atmosphere of 50 per cent relative humidity.

† From Ilford Research Laboratories (17).

The effects of pressure, temperature, humidity, etc. on emulsion properties and on latent image stability are described in detail by Beiser (4) and can be examined only briefly here.

*Temperature.*—The emulsion melting point is somewhere above 45°C. and the plates should, of course, not be exposed to excessive heat. The influence of temperature on sensitivity in Ilford G 5 emulsions was studied by Lord (23) who found the maximum sensitivity around 0°C. with slightly decreased sensitivity at higher and lower temperatures. The emulsion is still sensitive to minimum ionization at -60°C. It seems to have zero sensitivity at -200°C. The temperature effect may be higher in less sensitive emulsions (24).

*Pressure.*—Although early types of plates were quite sensitive to surface pressure, this is no longer the case. Upon request, some manufacturers have

added a thin coating of transparent gelatin to the surface of their plates as a protection against scratches etc. Plates can be exposed at low pressure and in vacuum, but the loss of humidity which then occurs can make the emulsion leave the glass, unless ordered from Ilford "with extra plasticizer" [some change in composition (20)] or dipped in a solution of glycerine [recommended by Eastman Kodak for their emulsions (15)]. The author exposed Ilford G 5 emulsions in nitrogen of 50 atmosphere pressure and more, without apparent effect.

*Humidity.*—The hygroscopic properties of gelatin make the density of emulsion depend on atmospheric humidity. The manufacturers supply data on the influence of humidity on their plates. The corresponding change in composition in emulsion thickness, in stopping power etc., must be taken into account for precision measurements. Humidity has also a slight influence on sensitivity.

*Contact.*—Contact with metal like copper, aluminum, iron, etc., fogs, or even decomposes the emulsion. A similar effect is observed when exposing the emulsion in hydrogen, in which case complete blackening of the plates occurs quite rapidly unless the plate is cooled to a sufficiently low temperature (25). It seems very difficult to find a thin coating which can be applied to the surface of the emulsions and through which hydrogen can not diffuse.

*Fading.*—The mechanism of the fading of the latent image with time and the influence of physical and chemical factors on this phenomenon were the subject of much research (4). Although fading is often negligible in minimum ionization emulsions, it is increased by higher temperature and humidity, so that such conditions should be avoided as much as possible during exposure and before development.

*Eradication.*—Accelerated fading is possibly the best available method for eradication of the latent image before exposure, but it is sometimes difficult to achieve without reducing the sensitivity of the plate. Albouy & Farragi (26) report that latent images in Ilford G 5 are destroyed without effect on sensitivity by heating for a few hours in a humid atmosphere at temperatures ranging from 60 to 90°C. The plates must, of course, be kept strictly horizontal. Other interesting results are those of Goldstein & Sherman (27) on the use of Herschel effect.

*Shrinkage.*—After processing, the thickness of the emulsion is changed and usually reduced by a factor of the order 2 or 3. This shrinkage sharply depends on the concentration of the glycerine bath used at the end of the processing (see below) and on the atmospheric humidity during observation (12). Various methods are available to measure this effect (28, 29).

Proper processing makes the images of minimum ionizing particle appear, in a sensitive emulsion, as rows of developed grains with densities of 20 to 30, or even more, grains per 100 $\mu$ . The visibility of these tracks depends on the ratio of the grain density of the tracks to the surrounding background of slow electrons and randomly developed grains (fog). Interesting studies of track recognition in varying conditions of grain and fog densities are given



by Coates (30), Berriman (31), and Beiser (32). More ionizing particles produce denser tracks: first with increased grain density, and then with the appearance of continuous strings of increasing width. The tracks are usually not straight lines, but show multiple scattering. Electrons can be ejected from atoms situated near the path of sufficiently high-energy or highly charged incident particles, and appear as individual  $\delta$ -rays. Slow particles often are brought to rest and end their range in the emulsion. Multiply charged particles capture electrons toward the end of their range, thus decreasing in effective charge and giving a characteristic tapered shape to their tracks. Quantitative measurement and theory of these phenomena are at the basis of the photographic emulsion technique, as they permit the determination over certain ranges, of the charge, mass and energy of the incident particles.

### PROCESSING

For all experiments where measurements need to be performed on the tracks and where a low background ( $\gamma$ -rays, electrons etc.) can be maintained, there is a premium in having long tracks, so that emulsions of great thickness must be used. The central problem of processing thick emulsions is to achieve an even development throughout the thickness and over the whole area of the plate, in spite of the fact that developers and other chemicals only penetrate by a relatively slow diffusion process from the surface. Other stringent requirements are a high contrast, i.e., the tracks easily recognizable from a background of random grains (fog as low as possible) with no coloration of the gelatin; and absence of distortion, so that to the highest degree of precision the developed grains reproduce the original paths of the charged particles. Distortion can occur in all stages of the processing, if proper precautions are not taken. It is essential, for instance, that the plates remain horizontal, that at no time strong gradients of concentration, or temperature exist in the emulsion or its vicinity, and that any osmotic pressure effects be reduced to a minimum. It is well known that the swelling of the gelatin is a function of its pH and, it may well be that the ideal development should be made in successive baths of constant pH. It is convenient to divide the processing technique in two steps: (a) the developing stage, where the plate is usually soaked in distilled water to allow some swelling, and then through suitable chemical action the sensitized silver bromide grains are reduced to metallic silver, after which the action of the developer is checked by a neutralizing agent; and (b) the after-developing stages including the fixing where the undeveloped opaque silver bromide is dissolved, the washing and the drying.

*Development.*—The simplest method to achieve even development of thick emulsions is perhaps to choose a slow developer with a long induction period. It penetrates throughout the thickness in a time appreciably less than the developing time itself. Standard x-ray film developer, like the D 19, fulfills this condition when suitably diluted for thicknesses up to 100

or 200 $\mu$ . Recently Summerfield (33) reported an extension of this simple method to thicknesses of up to 400 $\mu$  by using a relatively slow developer, and further slowing down its effects by reducing the temperature to 4°C. With this technique, developing, stopping and fixing are all done at the same low temperature with the additional advantage of keeping the gelatin in a relatively firm condition and thereby reducing the possibility of distortions.

The most widely used method to-day is the Temperature Development technique (TD) of Dilworth, Occhialini & Payne (34), further studied by numerous workers (35 to 42). The TD technique is based on the difference in temperature coefficients between diffusion and developing processes. A developer is chosen whose chemical effects are more reduced at low temperature than is its diffusion speed. The development begins by a bath in distilled water which produces a preliminary swelling of the gelatin and facilitates the subsequent diffusion of chemicals. The duration of this preliminary bath can be the same as that of the cold stage discussed below. The bath is slowly cooled. Then begins the "cold stage": The distilled water is replaced by a cold bath of the developer which is allowed to diffuse evenly throughout the thickness of the emulsion, while no appreciable development occurs. The plate is then taken out of the bath, the excess developer on its surface is gently wiped off, and during a "hot stage," the plate is slowly heated in a humid and sometimes inert (nitrogen) atmosphere up to a temperature where the chemical developing effects occur. The developer, imbedded in the gelatin, should then produce identical effects in all layers, in particular, the surface, not being in contact with fresh developer, does not receive preferential treatment. After a suitable time, the temperature is lowered to stop developing effects and the plate is immersed in a cold stop bath. This method has proved successful for thicknesses up to 1200 and even 2000 $\mu$ .

The requirements for a developer suitable for the temperature development technique are quite stringent and not easy to meet. Quick penetration through emulsion, moderate or high temperature coefficient, stability at high and at low temperature, negligible production of fog or stain, pH close to that of emulsion, no solvent effect for silver bromide, absence of oxidation by air are some of the conditions listed and examined by Dilworth, Occhialini & Vermaesen (35). Among the large number of known photographic developers there are certainly candidates for filling several of these requirements, but it is hard to find one that meets them all. Much research has already been devoted to this choice, and amidol (2:4 diaminophenol hydrochloride) seems to be the best available at present. It is used in a solution of proper preservative, restraining and buffering qualities, the composition of which may vary according to the thickness of emulsion processed. In particular, when thick emulsions are developed, the cold stage is very long, and the developer must have restraining properties not obtained with the usual addition of potassium bromide. More restraining effect can be obtained by making the solution slightly more acid. Two mild acidifying agents were

proposed for this purpose, boric acid (35) and sodium bisulphite (37) which also improve the buffering qualities of the developer solution. The composition of two of the more widely used developers is given in Table II. As they are rather rapidly oxidized by air, the developing solutions should be prepared immediately before use and only used once.

TABLE II  
COMPOSITION OF TYPICAL AMIDOL DEVELOPERS

	Brussels*	Bristol†
Amidol	4.5 gm.	3.0 gm.
Sodium sulfite (anhydrous)	18 gm.	6.7 gm.
Potassium bromide (10 per cent solution)	8 cm. <sup>3</sup>	
Boric acid	35 gm.	
Sodium bisulfite liquor (Specific gravity 1.34)		1.4 ml.
Distilled water	1000 ml.	930 ml.
pH	6.4	6.7

\* From Dilworth, Occhialini & Vermaesen (35).

† From Dainton, Gattiker & Lock (37).

The temperature of the cold stage does not seem to be very critical, most authors use 4 or 5°C. or less. The time required varies with thickness of emulsion. Dainton, Gattiker & Lock (37) measured penetration time of various developers, including amidol, in nuclear emulsions. However, longer times are usually recommended and a good working rule is 20 to 25 min. for each 100 $\mu$  of emulsion thickness. The temperature of the hot stage is very critical, and a slight change can produce an appreciable difference in degree of development. It is useful to control the rates of temperature rise and drop at the beginning and at the end of the hot stage to insure accurately reproducible results. These rates should not be too fast, otherwise distortion or even reticulation of the gelatin may occur. It is also found that the temperature needed for the hot stage varies with emulsion thickness, and also slightly from batch to batch. These properties necessitate use of apparatus to control temperature accurately and to insure even temperature distribution over the whole area of the plate. Proper choice of hot stage temperature affords a convenient method of obtaining any required degree of underdevelopment for special purposes. The boric acid type of amidol developer seems to require somewhat higher hot stage temperatures than the bisulphite type. Indeed, the bisulphite developer used at 10 or 14°C. for a long enough time provides enough development to show minimum ionization tracks in Ilford G 5 plates, although the grain density is not as high as may be desired [Herz (39)]. Herz & Edgar (41) point out the advantages of using a lower temperature for the hot stage: when the wet emulsion is warmed, it loses elasticity and becomes dough-like and sticky, stresses

are released if present, and when the emulsion is later dried, it has a much greater tendency to shrink in a direction parallel to the glass base than one which has been kept at a lower temperature throughout. The boric acid amidol and the temperature development technique produce images of very good contrast and extremely low amount of distortion when applied with proper care, using a hot stage temperature of about 28°C. for 30 min. to 1 hr. Alternatively, excellent results are also obtained by using a much lower hot stage temperature, of 8°C. to 14°C. for several hours, with the advantage that absence of distortion may be more easily achieved.

Special apparatus is needed to supply the solutions at required temperatures and to perform the necessary temperature changes with accuracy and reproducibility. For infrequent development of relatively few plates; one of the simplest of these, is a hermetic container of suitable geometric design to insure even heat transmission and temperature distribution, which can be immersed (with plates and solution inside) in successive water baths of suitable temperature. For frequent developments of large numbers of plates, in strict conditions, more elaborate apparatus are needed, such as that described by Dilworth *et al.* (35). Essentially it consists of a jacketed container for plates and solutions with an automatic device providing a circulation of water of controlled temperature in the jacket.

The composition of the stop-bath is not very critical. Usually a slight change in pH, making the plate more acid, is sufficient to stop completely developing effects, and very dilute acetic acid or sodium bisulphite is used. The duration of the stop-bath is governed, as the cold stage, by the time required for the diffusion process to take place, and again an empirical rule of 20 to 25 minutes for each 100 $\mu$  of emulsion thickness can be recommended.

*After development.*—After the stop-bath, it is convenient to remove the thin silver layer sometimes deposited on the emulsion surface by rubbing gently with a soft tissue, and the plate is then washed in running water of low temperature to eliminate as far as possible all remains of used developer and stop-bath. The plate is then ready for fixing. The fixing is amongst the most critical phases of processing, as the large fraction of undeveloped silver bromide must be dissolved and evacuated. "In the development stage, the emulsion, held firm only on the side of the glass, has the support of a hard skeleton of silver halide, whereas during fixing, washing and drying it is reduced to a soft jelly (43)." The choice of the composition of the fixing bath has received much attention as it appears to have a major influence on the final transparency of the plate. The basis of all fixing baths to date is sodium thiosulphate (hypo), used at about 40 per cent concentration. Dainton, Gattiker & Lock (37) and other authors (42) recommend the addition of sodium bisulphite, making the solution more acid and therefore reducing the swelling and to some extent the staining of the gelatin. This practice is not followed by Bonetti, Dilworth & Occhialini (43) who prefer not to decrease too much the pH of the hypo solution to avoid the risk of decomposition. They control the amount of swelling by observing the thickness of a control

test plate with each processing, and by the progressive addition of sodium sulphate up to about 10 per cent concentration. They use a bath of very dilute acetic acid to remove staining after the fixing is completed. A difficult question is that of agitation and solution renewal during fixing, as any excess of motion and any brutal change of concentrations may cause distortion, while complete absence of motion and local or total exhaustion of the solution increase the fixing time and the staining. Nitrogen bubbling can provide some agitation (36). An apparatus producing an even and gentle laminar flow of hypo above the plates is described by Bonetti, Dilworth & Occhialini (43).

It is essential to end the fixing by progressive dilution of the hypo at a very slow rate. Rapid changes of concentration at this stage are known to produce severe distortion and may even cause the emulsion to leave the glass. The dilution may start when the plate first looks transparent and, as dilution proceeds, fixing is progressively completed. It can sometimes be followed by a bath of dilute acetic acid which may help to reduce the staining. The plate can then be washed and is ready to dry. It is recommended, before drying the plates, to give them a bath in a solution of glycerine at a concentration

TABLE III

EXAMPLE OF TEMPERATURE DEVELOPMENT SCHEDULE FOR 600 MICRONS PLATE

Operation	Bath	Temperature	Time
Development			
Preliminary soaking	distilled water	cooling down to 5°C.	120 min.
Cold stage	boric acid amidol*	5°C.	120 min.
Warm stage			
slow heating	dry†	5°C. to 28°C.	5 min.
development	dry	28°C	60 min.
slow cooling	dry	28°C. to 5°C.	5 min.
Stop bath	acetic acid 0.2 per cent	5°C. to 14°C.	120 min.
Silver deposit cleaning‡			
After development.			
Washing	running water	14°C.	120 min.
Fixing	hypo 40 per cent§	14°C. cooling down to 5°C.	until clear
Slow dilution	water§	5°C.	100 hr.
Glycerine bath	glycerine 2 per cent	5°C. to ambient	120 min.
Drying		20°C.	7 days

\* See Table I.

† Wipe the plate surface with a soft tissue.

‡ Remove the silver deposited on the surface with a soft tissue.

§ Add sodium sulphate in increasing concentration up to 10 per cent if swelling is excessive.



of a few per cent. This will prevent the emulsion from becoming too dry (when the humidity of the laboratory atmosphere is low) and from breaking its glass backing. It is of interest to note that the degree of shrinkage of the emulsion strongly depends on the concentration of glycerine, so that it can be controlled adequately (44, 45).

The drying can be made by immersion in a succession of baths containing glycerine and alcohol in increasing concentration. If carried up to very high concentrations of alcohol, it may give unwanted hardness to the gelatin (43). The other method of drying relies on evaporation, its main difficulty is to achieve even evaporation over the whole area of the plate. This can be obtained by controlled slow air circulation, but special precautions are needed for the edges of the plate which have the tendency to dry first. The plates can be surrounded by a guard ring of dummy plates (43) or very large plates can be used of which an area near the edges is discarded (37). It is possible to use gentle infrared heating to help the process of drying (43). As an illustration, a typical development schedule for Ilford G 5 plates of 600 $\mu$  is given by Table III.

Several essential techniques cannot be discussed here in detail: developers giving a controlled degree of underdevelopment (46); developers selectively developing track images in a background of  $\gamma$ -rays (47, 48); a method for clearing overstained plates (49) (a result which can also sometimes be obtained by a new fixing after the plate is dried); a procedure for mounting stripped emulsions on glass, before processing (40, 50); and the quantitative measurements of distortion (51, 52).

#### OBSERVATION

Like all other experiments, those that can be performed with nuclear emulsions encounter some of their most severe limitations when they meet the limitations of the human being using them. He can only handle a limited amount of information over a given time and experiments must usually be done over a few months or years. Scarce are the experiments with plates where more than a few thousand tracks were examined. Observation of the plates under the microscope is, of course, where human limitations appear. Scanning of an emulsion to locate events requires long hours of patient observation and is usually entrusted to professional scanners, recruited from semi-skilled personnel and patiently taught to use the microscope, to recognize events and even to perform measurements. Scanners thus become extremely useful assistants and a group of well trained professional scanners may be the most valuable asset of many laboratories using the technique. Even with their help, physicists must spend hours at their microscope, looking at tiny details of the field of view, with head in a fixed position in front of the eye-pieces and steady hands delicately moving the mechanical controls of the instrument. This is often found too taxing and may be the main reason for the technique not having a still more extensive use.

Any improvement in microscope design is worth watching. Much re-



search effort has already been devoted to improvements of this instrument. Most of the microscopes available commercially are built for biology and medicine, with various degrees of mechanical perfection of the stage. Only the most perfected of these find their use for photographic emulsion technique and then, are not very well adapted except for the simplest operations, for instance, scanning and location of events. To perform measurements on the tracks the graduations of the stage are usually not precise enough and the motions are actuated by too coarse screws. It appears that, as for mechanical construction of microscopes, the domain of emulsion technique starts just about where the technique in medicine and biology stops. Microscope manufacturers have only just begun to explore this new domain. Some of them have supplied physicists with special accessories custom-built for a special need, such as a precision screw, allowing an accurate determination of distances (53). A remarkable pioneering design of microscope, specially built for nuclear emulsion technique, has been made by Cooke, Troughton & Simms, in England. Their model 4000 found, so to speak, its use mostly limited by price for a long time. It is still today one of the commercially available microscopes best adapted for emulsion work. Another special microscope is now being manufactured by Koristka, in Italy, based on Cosyns' principle (54), and especially suited for the measurement of multiple scattering. Other models were made or announced by Bausch & Lomb in the United States and Leitz in Germany. In the opinion of the author there is still room for much development of special microscopes for emulsion technique. This may be illustrated by reference to a number of convenient accessories that many authors have built themselves in laboratory workshops, such as tilting stages (55), or tilting microscope bodies (45), precision screws (56), recording devices (55, 57), goniometers of high accuracy (54), also stages with good rectilinear motion for measurement of scattering (54, 58). If some of these accessories, and perhaps others, could be perfected and made readily available to the users of emulsion technique, there is little doubt that they would soon find a relatively broad market.

Similar considerations apply to the optical system. The observation of thick emulsions requires objectives with medium or high magnification, flat field, large numerical aperture, and large working distance (distance between the object plane and the front lens). Several objectives meeting these requirements were successfully developed in recent years by Cooke ( $\times 45$ , n.a. 0.95, w.d. 1.5 mm.), Leitz ( $\times 53$ , n.a. 0.95, w.d. 1 mm.), Koristka ( $\times 55$ , n.a. 0.95, w.d. 1.35 mm.) and others. These are most useful for observation and measurements of selected events. For systematic scanning the need was long felt for an objective with low magnification and high numerical aperture using oil immersion. This need was recently filled by Leitz ( $\times 22$ , n.a. 0.65, w.d. 2.3 mm.) and Koristka ( $\times 30$ , n.a. 1.05, w.d. 3 mm.). These objectives solve the old difficulty of constantly changing from dry objective to oil immersion. In addition, the use of oil greatly improves visibility when, as is often the case, the surface of the emulsion is not perfectly smooth. New improvements

in optical systems are hoped for, such as a wider field of view at low power. It may be useful to remark that optical systems for nuclear emulsions can be designed without chromatic corrections, as the examination is easily made in monochromatic light.

Several attempts were made to make the microscope somewhat automatic. Successful instruments were built for limited purposes: to facilitate scanning (59, 60, 61), to record observation (57), or to make automatic measurements (62). One of the main difficulties in the task of making automatic microscopes may be to draw a line between the opposite requirements of versatility and mechanical simplicity. Another is to devise improvements that really relieve the task of the observer who must look at the tracks and guide the automaton. The most elaborate instrument recorded in the literature is perhaps that of Blau, Rudin & Lindenbaum (62). In spite of these very interesting efforts, few automatons were used for actual investigations in physics: an indication that the problem is difficult and that the field is still open for much progress.

The human eye has been replaced in measuring the density of tracks by a photometric device (described in Energy Loss and Measurements of Ionization). However, the eye has not been replaced in its role of locating events. Experiments have been performed in which the microscopic image is scanned with a television system thereby translating the field of view into a succession of electrical impulses (63, 64). This problem is made difficult by the high resolution needed and by the fact that the microscope itself is often used at the limit of the optical resolving power. Even if the scanning problem were satisfactorily solved, a computing mechanism is required to decide whether or not some of the grains among the many grains scattered over a field of view are aligned over the straight or slightly curved line of a track (63, 64), while even the most inexperienced eye will detect them at a glance. The same difficulty holds even more for the selection of a given type of complicated event. An electronic computer can probably be taught to recognize, say, a meson decay, but it will take much development and research before electro-mechanical scanning robots will contribute to advances in nuclear physics.

#### RANGE-ENERGY

The range of a charged particle brought to rest in the emulsion can be measured with high accuracy, and a considerable amount of theoretical and experimental work has been devoted to establish a precise range-energy relation. In principle, this relation can be calculated by integrating the Bethe (65) formula for energy loss, provided proper values of the average ionization potentials of the atoms are inserted. Improvements were made recently in the experimental knowledge of the potentials (66) and, in stopping power theory, in the calculation of the contribution of the K electrons (67, 68). A critical survey of their use for emulsion is made by Vigneron (69), who gives a semi-empirical treatment of the range-energy relation in excellent agreement with experiment. This calculation also agrees with earlier results,

based on the range-energy relation in air, and on a calculation of the ratio of stopping power between air and emulsion [Cüer (70), Webb (71), Wilkins (72)]. Extensive experiments have established the range-energy relation for protons and other singly charged nuclear particles. The early results of Lattes, Fowler & Cüer (73) were improved by Rotblat (74), Catala & Gibson (75), Nerenson & Reines (76), Cüer & Jung (77) and others (78, 79), and extended to higher energies by Bradner *et al.* (80). A range-energy curve for dry Ilford C 2 emulsion exposed in vacuum is given in Fig. 1. Plates in equilibrium with the atmosphere at average pressure and humidity exhibit ranges increased by 3 to 4 per cent (74). No appreciable change is found between different batches of emulsion of the same type, but the stopping powers of type Ilford E 1, Ilford G 5, and Kodak NT 2a are respectively 0.3 per cent lower, 1 per cent higher, and 1.8 per cent higher than that of Ilford C 2. Range-energy relations are given for Eastman NTA (81), for Eastman NTB (82), for diluted Ilford G 5 (83), and for Ilford C 2 plates soaked with water (4, 72). The experimental data for protons between 14 and 30 Mev are represented with an accuracy of the order of 2 per cent by the simple approximate formula (80)

$$E_{\text{Mev}} = 0.251R_{\mu}^{0.581}$$

which can probably be safely extrapolated to energies as high as 200 Mev, as checked indirectly by Gottstein & Mulvey (84).

From the proton range-energy curve  $R=f(E)$ , the range-energy relation for other singly charged particles of  $M$  proton masses is easily derived by the familiar relation  $R/M=f(E/M)$ . The somewhat different case of electrons was investigated by Ross & Zajac (85), Hertz (86), and Blum (87).

The range of particles of  $M$  proton masses and charge  $z$  can also be derived from the proton relation, after a correction to take into account the capture and loss of electrons which occur when the particle slows down to atomic electron velocities. From his experiments with  $\text{Li}^8$  and  $\text{Be}^8$  nuclei and by comparison with earlier values (72) on  $\alpha$  particles, Barkas (88) gives the following relation for light nuclei:  $z^2R/M=f(E/M)+0.12z^3$  valid for  $v/c > 1.04z/137$ . Somewhat different results are derived in a review by Longchamp (89). For heavier nuclei, the reader is referred, for instance, to the paper of Perkins (90).

It can be concluded that a precise measurement of ranges yields an accurate determination of particle energies. This holds true for the mean range of a group of monokinetic identical particles. For an individual track, a slight uncertainty is attributable to straggling. Values of the straggling, both resulting from statistical fluctuations in the slowing down process and distances between grains with finite size, are found, for instance, for C 2 emulsions (74). Straggling amounts to 10 per cent for 1 Mev protons with a decrease to 2 per cent for 5 Mev protons. At higher energies, straggling can usually be neglected being no greater than the uncertainty of the range-energy relation itself.

*Taper length.*—The ionization along tracks of multiply charged particles

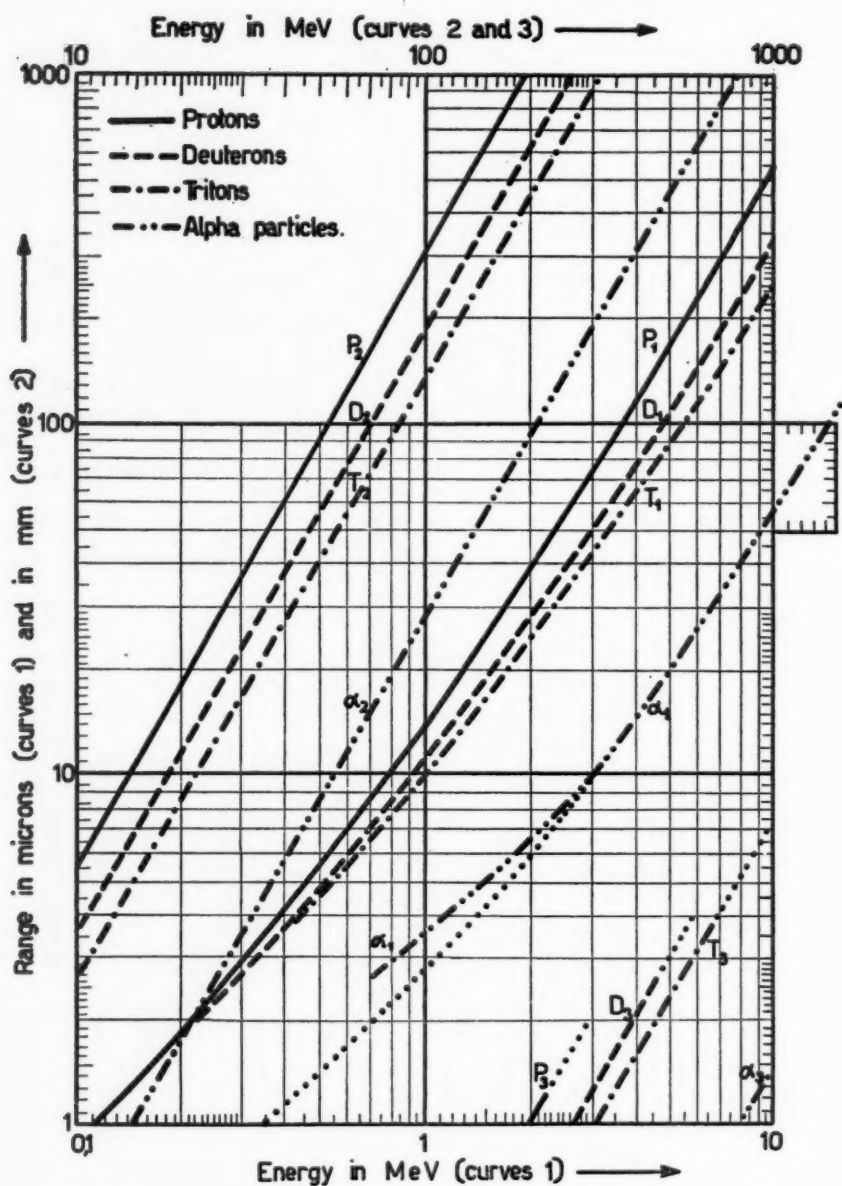


FIG. 1. Range energy relation for Ilford C 2 emulsion. From Vigneron (69).

show a characteristic taper at the end of their range corresponding to gradual loss of charge by electron capture (91). The taper length  $L$  can be expressed in function of the charge  $z$  by  $L = az^\alpha$ . The values for  $a$  and  $\alpha$  result from an analysis of the ionization and electron capture phenomena. Perkins (90) used  $a = 0.7$  and  $\alpha = 2$ , but experiments by Hoang (92) and supporting theoretical considerations of Cürer & Longchamp (93) indicate that  $\alpha$  is of the order of unity.

#### ENERGY LOSS AND MEASUREMENTS OF IONIZATION

It is most likely that only a small fraction of the energy lost by a charged particle traversing the emulsion is used for the production of latent images that can be brought out during the development. The number of developed grains is a function not only of the rate of energy loss but also of the sensitivity of the emulsion and of the nature and degree of development. Grain counting and other techniques, discussed in some detail below, can provide experimental determinations of the rate of energy loss, which then can be examined in the light of theory to give information on the velocity and charge of the particle responsible for the observed track.

For slow particle velocities, the rate of energy loss is given by the well known Bethe formula, already mentioned in connection with range-energy calculations. The rate of energy loss is proportional to the square of the particle charge and a function of the particle velocity (apart from a negligible correction). The formula shows a decrease in energy loss as the particle velocity increases, with a minimum occurring at an energy of about twice the particle rest mass. After the minimum, the energy loss rises logarithmically with particle energy.

It is well known since the work of Fermi (94) that the rate of energy loss of high velocity particles is affected by the polarization of the medium. Negligible at low energies, this effect becomes considerable for relativistic velocities. Instead of a logarithmic rise, the rate of energy loss is found to saturate at high energies, at a value depending on the dielectric properties of the medium, but usually not very much above the minimum. Improvements were brought to the Fermi theory by Wick (95), Halpern & Hall (96), and Bohr (97), using more refined representations of the dielectric properties of the medium. Examining the applications of these theories to the grain formation in emulsions, Messel & Ritson (98) and Schönberg (99) pointed out that, since the energy is lost by fast particles in two distinct processes, ionization excitation and emission of Cerenkov radiation, the contribution of these processes to latent image formation along the particle track will depend on the probability that energy lost in these two forms is captured in the silver bromide crystals. As for the ionization process, electrons ejected with high velocity will appear as  $\delta$ -rays with ranges much greater than the radius of the silver bromide crystals, in which they will spend only a small fraction of their energy. The energy lost in the form of such  $\delta$ -rays will not contribute to latent image formation on the track. The quantity to be used for com-

parison with observed grain density is not the total rate of energy loss, but the energy lost in all collision processes involving electron energies less than some maximum energy value  $E_{\max}$ . This quantity is little affected by the exact value of  $E_{\max}$  [evaluated to lie between 2 and 5 kev (98,100)]. Whereas the total increase predicted by theory in silver bromide amounts to about 30 per cent, the  $E_{\max}$  limitation reduces the increase to about 15 per cent (see Fig. 2). These authors further demonstrated that the remaining increase was entirely attributable to increasing Cerenkov emission. This radiation is

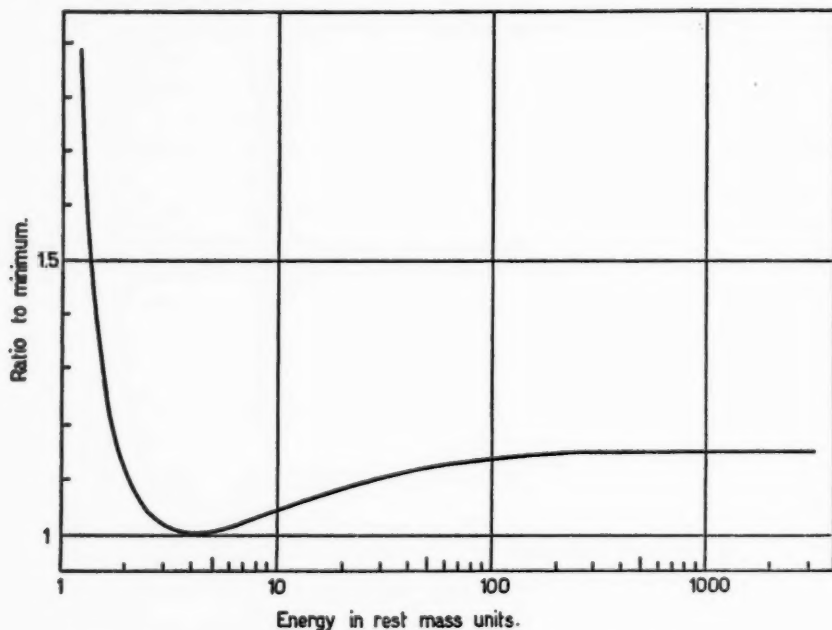


FIG. 2. Rate of energy loss in silver bromide in processes involving energy transfers of less than 5 kev., as a function of the particle energy. Calculated by Shapiro & Stiller (109) from results of Halpern & Hall (96) and Sternheimer (110).

emitted at frequencies in the neighborhood of resonance lines and is therefore strongly absorbed. But at least for the highest Cerenkov bands, it is very doubtful that the absorption coefficient would be high enough to stop the radiation from leaving the silver bromide crystals. Specific calculations on Cerenkov radiation capture in the crystals of silver bromide were made by Janssens & Huybrechts (100) following the theory of Schönberg, with the conclusion that only a small fraction was captured. Thus they were led to the conclusion that practically no increase in grain density was expected after the minimum.

This result seemed in agreement within experimental errors with early measurements (101, 102) but was not further confirmed experimentally.



Careful observations of the grain densities of fast electrons, mesons and protons established a definite increase of grain density between a minimum at about 2 rest masses and a plateau at high energies. Although the experimental errors are still appreciable, the results are not entirely consistent in two respects: the amount of increase and the value of the energy at which saturation is reached. Thus Pickup & Voyvodic (103) observing fast electrons, first measured a rise of about 10 per cent to a plateau starting at an energy of about 20 rest masses. These very preliminary results were later improved by observations of Morrish (104) on fast electrons, who detected a rise of about 5 per cent between 9 and 25 rest masses, a result consistent with later measurements of Voyvodic (105) on  $\pi$ -mesons and electrons, and of Daniel *et al.* (106) on cosmic ray particles. [See also Jauneau & Hug-Boussier (107) and Danyasz, Lock & Yekutieli (108).] Other experiments on cosmic rays by Shapiro & Stiller (109), however, show an increase to a plateau at 12 to 14 per cent above minimum, reached only at energies as high as 100 rest masses. Several theoretical interpretations of the rise were given recently. Using Fermi's theory, Sternheimer (111) finds that only a small fraction of the Cerenkov radiation can escape from the silver bromide crystals, a result in contradiction with the calculations of Janssens & Huybrechts (100). Along similar lines, and taking into account the finite widths of the resonance frequencies of the medium, Budini's (112) results, depending sharply on the ratio between the width of the Cerenkov bands and the density of the medium, can be brought in good agreement with Morrish's (104) results. Huybrechts & Schönberg (113), taking more radical steps, show that in Fermi's method, the solution used for the fields at large distances depend quite strongly on the polarization of the medium in the immediate neighborhood of the track. They give a modification of Fermi's theory and their results also seem to be in agreement with Morrish's (104) observations and with the measurements of Gosh, Jones & Wilson (114) on the ionization of very fast particles in oxygen. In examining these results it is useful to remember, as indicated by Occhialini (101), that the relation of grain count to ionization also should be very closely studied experimentally in the region immediately before the minimum, and that part of the observed variation of grain density before and after the minimum may correspond to some mechanism specific to grain formation. The existence of the increase in principle extends the possibility of particle discrimination up to about 20 rest masses or more. The increase is however so small that reliability of measurements can only be obtained in very controlled conditions of image development and counting technique.

For low grain densities, grains only rarely cluster together and best reliability in counting is usually obtained by so called "blob counting" (i.e., counting each cluster as one grain regardless of shape). This can usually be done up to 1.5 times the minimum. When tracks of higher grain density are counted, this method obviously no longer can be used and some convention must be made on how to resolve clusters of irregular shapes into number

of grains. For instance, a number of grains is assigned to a group in proportion to its length (2). An interesting statistical study of grain counting is given by Hodgson (115) who shows that the statistical distribution of grains is slightly more peaked than a normal distribution because of finite grain size, an effect analogous to counting losses in Geiger-Müller tubes attributable to finite resolving time [see also (116)]. This apparent slight increase in the precision expected from grain counting usually cannot be exploited, because variations in grain count throughout the thickness or over the area of any single plate are difficult to avoid, even with the most refined developing techniques (35, 104, 109) and even more so between different plates.

For high grain densities it is sometimes useful (117, 118, 119) to measure the ratio of length occupied by gaps to the length of a fraction of track. This determination may be less easily affected by personal errors than grain counting.

A very promising recent development is the replacement of the eye by a photometric device for evaluation of dense ionization. Von Friesen & Kristiansson (120, 121) describe a simple photometric method where the image of the track is focussed upon a slit corresponding to a field about  $1.5\mu$  wide and  $30\mu$  long. The light passing through the slit falls on the cathode of a photomultiplier tube connected to a galvanometer. Readings are taken alternately on the track and on the background on both sides, and a value of the track blackening is obtained from their comparison. This quantity is found to be a reliable function of the energy loss for high ionizations (above 4 times minimum). While the photometric method is convenient for emulsions of thicknesses up to  $200\mu$ , it is more difficult to use for thick emulsions, because light coming from an object situated at the bottom of the emulsion is scattered and diffused in the top layers resulting in a marked variation of contrast with thickness. Rather important corrections must be made to compensate for this effect, an example of which will be found in (122). Variants of the methods are reported by several authors (123 to 125). Ceccarelli & Zorn (126) used a similar photometric arrangement to measure the width of the tracks. Using a narrower slit and moving it in a direction transverse to the track, they show that the shape of the blackening distribution across the track is practically unaffected by the amount of ionization, while the half-width of this distribution is a reliable function of ionization. The measurements are not sensitive to emulsion thickness. This variant of the photometric technique is more specially suited for the very high-energy loss of multiply charged particles.

Measurements of high ionization by grain counting can be successfully made over a limited range, selected by choosing emulsions of adequate low sensitivity and by precise control of the degree of underdevelopment. Experiments using this method and details of application cannot be discussed here, but the reader will find examples in experiments on the neutron disintegration of lithium (127, 128) and boron (35) and in studies of the heavy primaries of the cosmic ray radiation (14, 129). Recently, Ilford announced the production of plates with alternate layers of G 5 emulsion and of a new,

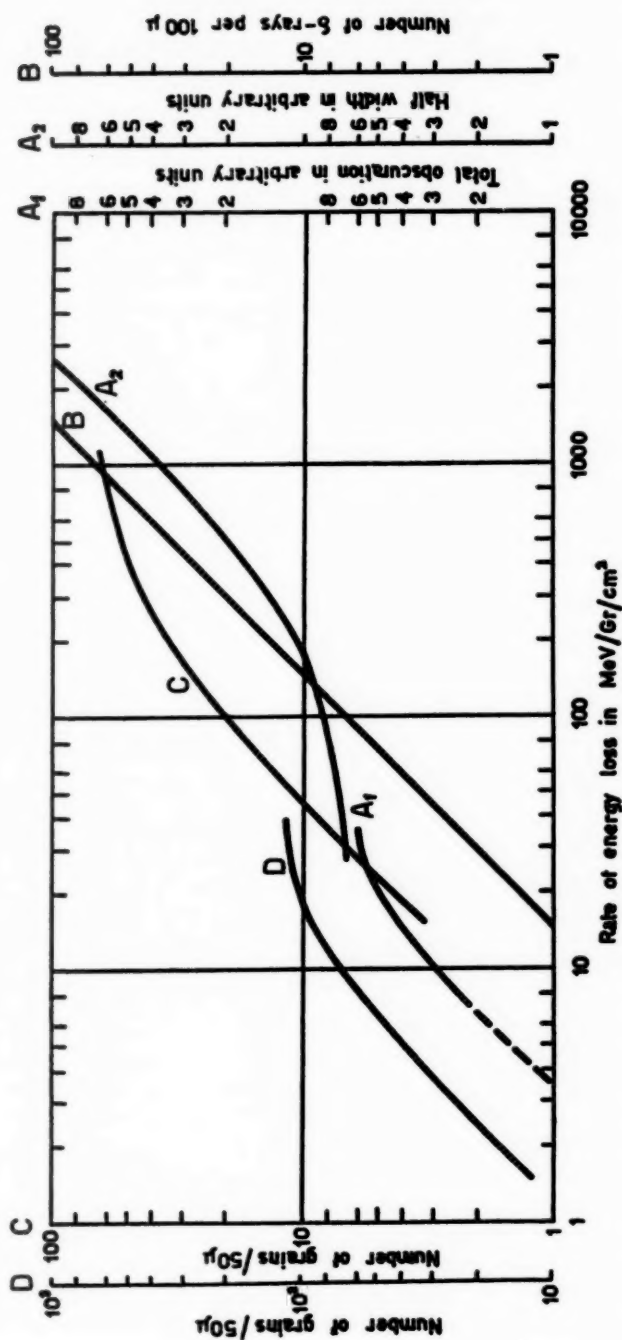


FIG. 3. Comparison of methods for the measurement of energy loss. From Ceccarelli & Zorn (126). A<sub>1</sub> Total obscuration, Ilford G 5. A<sub>2</sub> Half-width, Ilford G 5. B. Density of δ-rays (more than 3 grains) Ilford G 5 from (131). C. Grain density in underdeveloped Kodak NTA from (129). D. Grain density in Ilford G 5 (149).

low sensitivity G 0 emulsion, adapted for use with processing methods usual for G 5 (20, 130). An indication of the ranges of applicability of the various methods for the measurement of ionization are given by Fig. 3.

*Delta ray counting.*—Particles of sufficiently high velocity or charge eject electrons from the atoms of the emulsion with energy high enough to make them appear as independent tracks originating usually at an angle of about  $90^\circ$ . The frequency of these  $\delta$ -rays is discussed by Bradt & Peters (129) and, apart from a correction shown to be negligible for charges less than 30, is given by the formula: (when the atomic velocities of the electrons of the medium are neglected)

$$n = 2\pi N \left( \frac{e^2}{mc^2} \right)^2 \frac{z^2}{\beta^2} \left( \frac{mc^2}{E_1} - \frac{mc^2}{E_2} \right)$$

where  $n$  is the number of  $\delta$ -rays per unit length of track,  $N$  is the number of electrons (of mass  $m$ ) per unit volume of emulsion, and  $z$  and  $\beta = v/c$  are the particle charge and velocity.  $E_1$  and  $E_2$  are, respectively, the lowest and highest electron energies that will produce observable tracks. For slow particles,  $E_2$  is the maximum transferable energy  $2mc^2\beta^2$ . Emulsion sensitivity defines the value of  $E_1$ , and of  $E_2$  for fast particles, but not in a very critical way. In Ilford C 2 emulsion  $E_1 = 10$  to 15 kev, depending on the convention used for electron track recognition (for instance, that they should have at least 4 grains) and  $E_2 = 30$  kev. In Ilford G 5 emulsion,  $E_1$  is again about 10 kev, and  $E_2$ , mainly limited by the difficulty of recognizing electron tracks of low grain density and high scattering, is about 75 kev (129, 131). It is seen that as the  $\delta$ -ray density depends on the square of the charge and on the particle velocity, it offers an interesting method of measurement for high charges, slow velocities, or both.

In early systematic use of  $\delta$ -ray counting in the less sensitive Ilford C 2 emulsion, the observed number of  $\delta$ -rays was a fraction only of the theoretical number, as they could only be observed when they were lying almost parallel to the plane of the emulsion. Careful investigations on the tracks of slow particles with Ilford G 5 emulsions showed very good agreement with theory (132). But for fast particles, recent observation of Dainton, Fowler & Kent (131) do not seem to be in agreement with the above formula. Comparing the  $\delta$ -ray counts on slow protons and relativistic  $\alpha$ -particles, they obtained evidence for the proportionality between  $\delta$ -ray count and grain count. Their direct experimental evidence is limited to the region  $\beta < 0.54$ . In the opinion of these authors, however, indirect evidence for the validity of their law for higher values of  $\beta$  results from its application to a study of the presence of the lighter elements (Li, Be, B) in the multiply charged component of the cosmic ray radiation at high altitude. In contrast with the theoretical formula, their empirical relation resolves the charge spectrum into distinct peaks corresponding to these elements, in appreciable intensity. The existence of these light elements in cosmic rays is, however, the subject of contradictory results (14, 131), a controversy that cannot be examined here. It is clear that direct supporting experimental or theoretical results would be most useful in the high-energy region.

## MULTIPLE SCATTERING

The theory of the measurement of scattering in the tracks of particles passing through nuclear emulsion comprises three somewhat distinct problems: the differential cross section for individual single scatterings, the statistical combination of the successive single scatterings into a multiple deflection probability function, and the analysis of a sample (a few measurements) in terms of the multiple scattering distribution function and of the experimental errors of measurement.

The potential of the nuclei responsible for scattering is not a pure Coulomb field. At large distances it is modified by the screening effect of the orbital electrons, at short distances the finite size of the nucleus (and the possibility of nuclear interaction) must be taken into account. The effect of screening was investigated in detail by Molière (133) with a Thomas-Fermi approximation of the atomic potential. His expression of the differential cross section for single scattering is valid for all velocities and charges, and agrees with the previous asymptotic formulae of Williams (134).

It is customary to measure the deflections projected on a plane, usually the plane of the emulsion itself. The combined effects of the large number of single scatterings suffered by a particle traversing a given thickness of material give rise, in first approximation, to a Gaussian distribution of projected deflections [Fermi (135)]. A better approximation [Williams (134)] takes into account the relatively high probability of large single scattering (more frequent than a number of small scatterings adding up to a large angle). It adds to a central Gaussian distribution a "tail" of relatively high probabilities for large angles. The exact distribution function is now available from the work of Molière (133), Snyder & Scott (136), Goudsmit & Saunderson (137), as applied by Berger (138) [see also Sauter & Wanke (139)]. Comparisons between these various treatments are found in (140 to 146). The effect of the finite size of the nucleus on the shape of the distribution was recently investigated by Olbert (145).

The quantity which is usually compared with experiments and called "the mean angle of scattering" is the arithmetic mean of the absolute value of the angles of deflection corresponding to a number of traversals of equal thicknesses of material. It has become customary to express the theoretical results in terms of the mean angle  $\langle\alpha\rangle$  (in degrees) between successive chords to the track by the formula:

$$\langle\alpha\rangle = K(z/pv)(t/100)^{1/2}$$

where  $pv$ , the product of the particle momentum and velocity, is expressed in Mev,  $z$ , its charge, is in electron charges,  $t$ , the thickness of traversed material, is in microns, and  $K$  is called the scattering factor. The scattering factor  $K$  is a slowly varying function of the thickness  $t$  and, to a lesser degree, of the particle velocity  $v$  and charge  $z$ ; for instance, for  $v=c$  and  $t=100$ ,  $K=25.8$  in Ilford G 5 emulsion (146). The various theories quoted give values of  $K$  which agree within 1 per cent, when Molière's expression for the single scattering differential cross section is inserted (140 to 146). It

is seen that the measurement of the mean angle of scattering gives a direct evaluation of  $z/pv$ . In contrast with other determinations that can be performed on the tracks, it gives information on the particle energy (or energy per nucleon) even in the relativistic region. Thus energies can be evaluated up to  $10^{10}$  or  $10^{11}$  ev with remarkable accuracy, provided long tracks are available (several mm.).

Ideally, the multiple scattering is determined by measuring the angles between successive tangents to the track at regular intervals. In the actual case, exact tangents cannot be drawn, as the track is defined only by a number of developed grains of finite size unevenly spaced and not necessarily centered on the exact trajectory. To overcome this difficulty, two experimental methods have been used, which can be termed the "angular" method and the "sagitta" or "coordinate" method. In the angular method (147) the average direction of the track over a certain segment  $a$  is determined by fitting a straight line as closely as possible to the centers of gravity of the grains in the segment. This operation is repeated at regular intervals  $t$  (usually called "cells"). Replacing the exact tangents by such average directions corresponds to a certain "smoothing" of the scattered angles, reducing the mean angle of scattering in a ratio depending on  $a/t$ . For the limit  $a \ll t$  the best fitted line is close to a tangent and the smoothing factor is unity. For the other limit  $a = t$  (angles between successive best fitted lines) Molière (148) has shown in the Gaussian approximation that the smoothing factor is  $(26/35)^{1/2}$ . Intermediate cases are also given by Molière. In the coordinate method (149) the track is lined along a straight reference line (one of the rectilinear motions of the microscope stage, say  $x$ ). In principle, the distance between the line and the track is accurately measured at regular intervals. (Readings are taken of the coordinate  $y$  with a precise eye-piece micrometer.) It is easily shown that the second differences between the successive readings are proportional to the angles between successive chords of the track. In the Gaussian approximation, the mean angle between the successive chords is  $(2/3)^{1/2}$  of that between tangents, but a more precise determination of mean chord angle is given by Scott (146), Berger (138), and Molière (133, 148).

Several types of errors can be recognized in the measurement. The finite length of the track limits the number of statistically independent readings (statistical error). The finite size of the grains and their distribution give a spurious scattering or "grain noise." Imperfections of the microscope stage may not allow a motion of the track strictly parallel to itself in the angular method, or on a perfect straight line in the sagitta method ("stage noise"). The readings are made with a certain personal error. Finally, emulsion distortion can appreciably influence the results. Much work has been devoted to the study and elimination of these various sources of error. Stages of high accuracy were designed (54), stage noise was determined by observation of almost straight tracks (150) or by optical and interferometric control (54). Personal errors in reading are eliminated by perfecting the reading instru-



ment (54) or by repeated measurements. Improvements in processing methods were aimed at reducing the distortion. Noise and true scattering are different functions of cell length and series of measurements with various cell lengths can be compared to separate true and spurious scattering (141, 151). While the angles between successive tangents are statistically independent, a correlation between successive measurements of these angles exists because of measuring errors (148, 152, 153). A statistical method can be used to evaluate the correlation of the experimental measurements and thus to eliminate the influence of the errors. The same procedure may be applied to the somewhat more elaborate case of sagitta measurements. The ratio between true and spurious scattering imposes the choice of the cell lengths which must increase with increasing particle velocity and momentum. Thus the number of cells drawn on a track of finite length is limited and fixes the value of the statistical error. It is tempting to try to augment the accuracy by using overlapping cells. This procedure has received much attention (148, 154, 155), as the successive readings are statistically correlated and their analysis poses interesting statistical problems; but it appears that the advantage of using the technique of overlap is rather small. More fruitful is the method of Mabroux (156) in which the angle of scattering projected on a plane perpendicular to the plane of the emulsion is measured by a precision control of the vertical motion of the objective: these measurements are completely independent of measurements in the plane of the emulsion.

The tail of the scattering distribution has an influence on the analysis of observations. For instance, the presence of one large angle among a set of readings may appreciably contribute to the observed mean angle. It is shown that the statistical error affecting the result can be reduced, if such large angles are eliminated in a consistent fashion. A common procedure is to eliminate by cut and try all observed angles larger than four times the mean. Other methods were also proposed (157). The theoretical value of the mean angle of a distribution cut-off at four times the mean, is given by numerous authors (146). It is found to be about 11 per cent below the mean angle of the full distribution, while about 1 per cent of the angles lie above the cut-off.

A number of investigations have been devoted to comparing theory and observations by measuring the scattering of particles of known energy. Monokinetic electrons were used by Corson (158), Menon, O'Ceallaigh & Rochat (157), and Voyvodic & Pickup (142), while the scattering of fast protons was calibrated by Gottstein & Mulvey (159) and Berger (138). Measurements were made by Bosley & Muirhead (160) in diluted G 5 emulsions. Most of the results are reviewed in (138, 141) and show a satisfactory agreement between theory and experiment. The theory of Molière has also received good experimental support by other methods (161). One measurement on slow electrons in photographic plates shows, however, an appreciable discrepancy [Hisdal (144)].

## COMBINATION OF TECHNIQUES

*Singly charged particles.*—A particle producing a track in a nuclear emulsion must usually be identified as for mass, charge (possibly with sign) and energy. In principle, three independent measurements are needed to determine these three quantities. As the energy loss varies with the square of the charge, singly charged particles are easily recognized and two measurements ascertain their mass and energy. It is of course an essential feature of the nuclear emulsion method that some of the unstable particles can be recognized by their characteristic decay or interaction at the end of their range, but the discussion of these cases is outside the scope of the present review.

The combination range and ionization is of necessity limited to particles coming to rest in the emulsion. The variation of grain density (or gap density) with range was used, in early measurements of the mass ratio between  $\pi$  and  $\mu$  mesons (162), where a detailed account of the method is found. The technique is still useful for the rare and interesting observations of heavy mesons ( $\tau$ ,  $\chi$ ,  $\kappa$  . . .) where it affords a determination of their mass (163). A photometric determination for such an event is found in (122). The measurement of scattering versus range is also limited to tracks stopped in the emulsion. It has the advantage over the previous combination of being more independent of the emulsion sensitivity and amount of development, but for short tracks it is affected by a larger statistical error. The measurement was also used in early determinations of meson masses (147) and is also useful for the analysis of heavy meson events (163). The method was put in a very convenient form by Menon & Rochat (164), who obtain a satisfactory

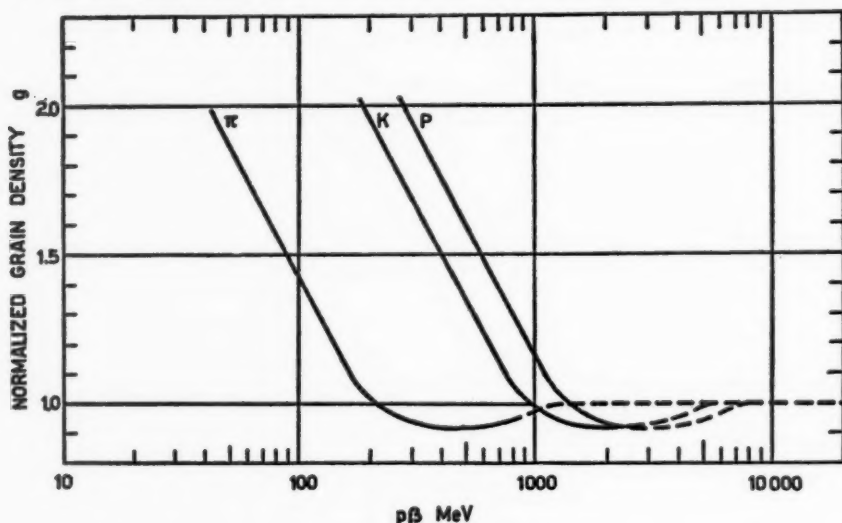


FIG. 4. The relation between grain density and  $p\beta$  given by a measurement of scattering for singly charged particles. The dotted part of the curve shows where the rise of ionization after the minimum may affect particle identification (106).

discrimination between slow mesons, protons, deuterons, and tritons. When the minimum ionization sensitive emulsions first became available, it was soon recognized (101) that the combined measurements of grain count and scattering would be the most powerful means of investigating the many high-energy tracks occurring, for instance, in cosmic ray stars. A large fraction of our present knowledge of these events is based on such measurements [see for instance (13)]. The range of energies in which good discrimination is obtained between particles of different masses critically depends on the amount of increase in grain density after the minimum, discussed previously (Fig. 4). Many of the most interesting disintegrations observed in plates exposed to cosmic rays at high altitude involve particles having energies equal to several times their rest masses. Most of the improved methods of grain count and scattering measurements are aimed at a better investigation of these events. For lower energies, grain counting can be replaced by gap measurements in combination with multiple scattering (165).

Deviation of relatively slow particles in a magnetic field in air or in vacuum, and subsequent recording of their directions and ranges in photographic emulsions were used in numerous experiments [see for instance (4, 10)]. Thus the charge of the particle is readily determined, and very good accuracy is obtained for mass measurements. In the emulsion itself, the curvature of fast tracks by a strong magnetic field was successfully observed by

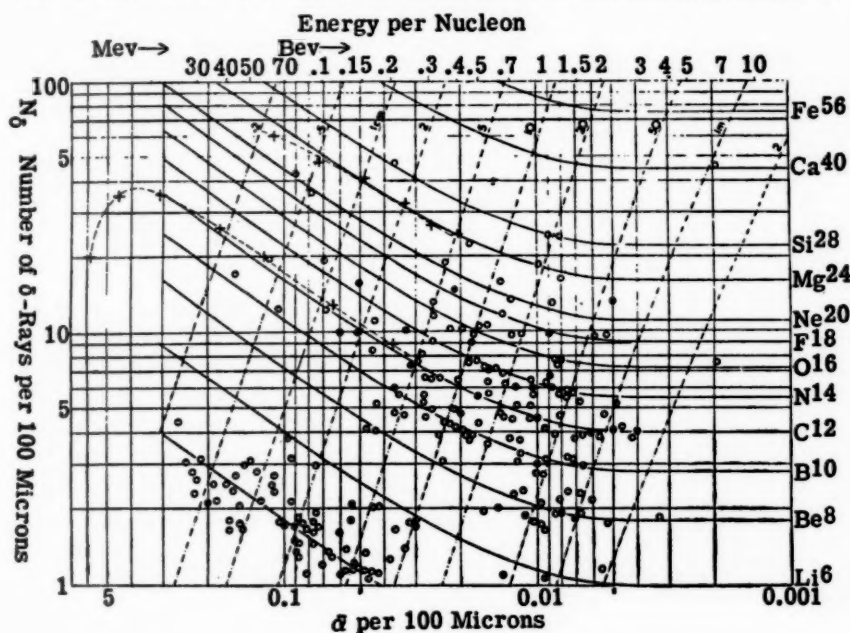


FIG. 5. The relation between  $\delta$ -ray count, multiple scattering and range (dotted lines) for multiply charged particles. In calculating this chart Dainton, Fowler & Kent (131) used their empirical relation for  $\delta$ -ray density.

Dilworth *et al.* (1966). The relatively high multiple scattering masks the magnetic curvature unless very high fields and sufficiently long tracks are used. When the direction of motion of the observed particle is known, the sign of the charge is determined with a certain probability. For instance, with a field of 34,000 gauss, the sign will be determined correctly for about 80 per cent of the tracks of 5 mm. length and for 90 per cent of the tracks of 1 cm. Examples of the use of this technique for the study of high-energy cosmic ray events are given in (167, 168).

*Multiply charged particles.*—For multiply charged particles it has been possible in most experiments to use the approximation of the mass being nearly equal to twice the charge. Two independent measurements are again sufficient, in principle, to determine charge and energy.

For particles coming to rest in the emulsion, the charge can be deduced from the taper length, or from the characteristic increase in  $\delta$ -ray density somewhat before the end of the range. Insensitive emulsions can be used to determine the ionization. Curves will be found in (14) giving the ionization and the  $\delta$ -ray density as a function of the range and the charge. Discussions of the precision that can be obtained by these methods will be found in (14, 92). For particles in the relativistic range, a measurement of  $\delta$ -ray density, or of ionization, determines uniquely the charge. The wider range of applicability of the  $\delta$ -ray count can be seen in Fig. 3, but it is less accurate than the measurements of ionization in insensitive plates, which is probably preferable for  $z < 6$ . A measurement of multiple scattering gives a value of the energy per nucleon. Fig. 5 graph indicates the region where measurements of multiple scattering,  $\delta$ -ray count, and range can be combined.

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# RADIATION CHEMISTRY<sup>1</sup>

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This article presents a survey of the field of radiation chemistry with emphasis on the physical point of view. It is concerned mainly with mechanisms and principles.

In the literature of radiation chemistry there are: recent review articles by Burton (1, 2), Dainton *et al.* (3, 4), Allen (5), and Weiss (6); reports of symposia held on radiation chemistry and related topics at Notre Dame (7), Oberlin (8), Army Chemical Center (9), Paris (10), London (11), Cleveland (12), and Leeds (13); books by Lind (14) and Lea (15); and, finally, numerous miscellaneous papers scattered throughout the literature. The bibliography of this article is, of necessity, far from complete, but we hope that a balanced picture of the subject is given.

## RADIATION EFFECTS AND RADIATION CHEMISTRY

For radiation energies of major interest in radiation chemistry, the only important interactions between radiation and matter are those resulting in transfer of energy to recoil electrons and recoil nuclei. It is convenient to divide radiation effects into two categories: (a) effects of ionization and electronic excitation; and (b) effects of atomic displacement.

Generally speaking, systems in which the first class of effects dominate are also those in which significant chemical changes result from radiation and they are the systems usually studied in "radiation chemistry." All systems in which molecular structure is important fall into this class. This paper is concerned with mechanisms of chemical change induced by radiation in such systems.

Systems in which atomic displacement is the dominant mechanism of radiation-induced change are usually solids with crystalline lattice structure in which there is no significant molecular unit. Changes effected by radiation in these systems are usually classed as physical (tensile strength, electrical, and thermal conductivity, etc.) rather than chemical. The term "discomposition" (1, 16) has been suggested to describe such changes; "radiation damage" (17) is also used. Wigner first called attention to the effect of atomic displacements and it is sometimes called the "Wigner effect" (1, 16, 18).

<sup>1</sup> The survey of literature pertaining to this review was concluded in February, 1953.

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The subject has recently been reviewed by Dienes (18) and Slater (17), and a basic discussion of the theory has been presented by Seitz (19).

The direct displacement of an atom from a molecule does, of course, lead to chemical change. It is usually ignored in radiation chemistry because it furnishes such a small fraction of the total chemical change. Platzman (20) has considered the effect in some detail for systems composed of light atoms (H, C, O, N) for incident protons and alpha particles in the 5 Mev range, and finds that roughly 0.05 to 0.10 per cent of the absorbed energy goes into atomic displacements. The ratio of ionizations to atomic displacements is, therefore,  $10^3$  or so, and since each ionization is likely to lead to chemical change, the displacement effect is too small to distinguish experimentally. Of course, for irradiation with  $\gamma$ -rays and electrons the displacement effect is even less important (17, 18, 19).

Lack of space in this review prevents an exhaustive treatment of all effects classed under radiation chemistry. We have attempted to present the principal mechanisms involved in the chemical action attributable to irradiation with sources in common use, such as  $\gamma$ -rays, electrons,  $\alpha$ -particles,  $\beta$ -particles, etc. Among the topics omitted is the special field of chemical effects following nuclear transformation, which is reviewed in this volume by Willard.

#### NATURE OF CHEMICAL EFFECTS

In general, chemical change results from utilization of electronic excitation energy in the dissociation or rearrangement of molecules. Electronic excitations are formed directly in impact processes and can also appear at several stages of the cycle in which ionizations are first formed and then neutralized. A general chemical reaction scheme, applicable in all cases, does not exist. The first attempt to apply modern ideas of chemical kinetics and molecular structure to radiation chemistry was made by Eyring, Hirschfelder & Taylor (21), and subsequent investigations have been strongly influenced by this pioneer effort (1, 2).

The radiolysis of hydrogen bromide gas, investigated by Lind & Livingston (22), furnishes a convenient example. The mechanism was considered theoretically by Eyring, Hirschfelder & Taylor (23), and a recent experimental study has been made by Zubler, Hamill & Williams (24). The result of radiolysis is essentially the same for  $\alpha$ -particle, x- or  $\gamma$ -radiation, and the over-all reaction can be written



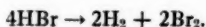
In terms of a possible detailed mechanism, five separate steps can be distinguished.

- (a) Ionization:<sup>3</sup>  $\text{HBr} \rightsquigarrow \text{HBr}^+ + e$
- (b) Electron capture:  $\text{HBr} + e \rightarrow \text{H} + \text{Br}^-$

<sup>3</sup> The symbol  $\rightsquigarrow$  is read "under high-energy radiation gives."

- (c) Charge neutralization:  $\text{Br}^- + \text{HBr}^+ \rightarrow \text{H} + \text{Br}_2$   
(d) Radical reaction:  $\text{H} + \text{HBr} \rightarrow \text{H}_2 + \text{Br}$   
(e) Atom recombination:  $\text{Br} + \text{Br} \rightarrow \text{Br}_2$

The omitted reaction  $\text{Br} + \text{HBr} \rightarrow \text{H} + \text{Br}_2$  is endothermic and will not occur at low temperatures. For each ionized HBr molecule, the mechanism yields four molecules of HBr decomposed, a fact which is verified by the addition  $(a) + (b) + (c) + 2(d) + (e)$ .



It is observed experimentally that almost exactly four molecules of HBr decompose for every ion formed under a wide range of conditions, a fact which supports this mechanism. It is, however, easy to demonstrate that the mechanism is somewhat more complicated. If, for example, instead of pure HBr gas, a mixture of HBr plus a rare gas (say at a ratio of one to fifty) is used, the yield is still about four molecules of HBr decomposed per ion pair formed, including all ionizations in the inert gas (24). For the rare gases helium or argon it can be presumed that all positive charges formed in the rare gas are transferred to HBr in collisions, since HBr has a lower ionization potential, and then the reaction continues according to the above scheme. On the other hand, xenon cannot give up its charge to HBr, because of an unfavorable ionization potential, but chemical change results nonetheless. A possible explanation (24) is that the polar HBr molecules form complexes with  $\text{Xe}^+$  ions and that the chemical change of reaction (c) occurs with such complexed positive ions. If this explanation is correct, complexing may also occur in the cases of helium and argon, rather than simple charge transfer.

The importance of the ion pair yield in gas reactions has been emphasized by Lind (14, 25). Excited molecules frequently do not seem to be involved. In the early days of radiation chemistry, all yields were described in terms of M/N values, i.e. the number of reacting molecules (M) per ion pairs formed (N). In the above example M/N is four.

The M/N method for reporting yields has been almost universally replaced in more recent work by the "G value" (16), which is the number of reacting molecules per one hundred electron volts energy absorbed. There are several reasons for preference of G values. First, it is not always known how many ion pairs have been formed, particularly in condensed systems (26), whereas the G value is the quantity actually observed. Secondly, it is unlikely that mechanisms are often dominated by ionic reactions as in the above example and there is no reason for expecting excited molecules to be generally ineffective. Finally, radical chain reactions frequently prohibit a simple interpretation of M/N.

#### THE ELEMENTARY PROCESSES

The primary interest in radiation chemistry is in chemical effects, and thus it is convenient to classify all elementary processes with respect to the condition of the molecules involved. The chemical state of a system is de-

scribed by its instantaneous chemical composition. Under irradiation, unstable intermediates are formed and their behavior determines the net chemical effects. Two distinctly different kinds of intermediates can be recognized: (a) those which have an unusual electronic condition, such as electronic excitation, net positive or negative charge; (b) those which are in a chemically unstable condition, for example atoms, radicals or very reactive molecules. The rates of formation and destruction of any intermediate determine its transient concentration. Presumably, if all rate constants were known, the radiation chemistry of a system could be predicted by a straightforward, if tedious, calculation.

*Formation of excited electronic states in impact processes.*—An excellent general reference on electronic and ionic impact processes is the recent book of Massey & Burhop (27). The theory of Bethe (28) predicts that excited states of molecules which result from very fast (primary) particle impacts are principally the optically allowed states. Fano (29) has emphasized that the extent to which each of these states is excited is in proportion to the oscillator strength of the transition. A study of molecular oscillator strengths has been made by Mulliken (30) and Mulliken & Rieke (31). These authors find that the molecular orbital method, and particularly the LCAO approximation, is rather good for the calculation of oscillator strengths of simple molecules. This fact may be very significant in connection with the well-known success of the Bragg rule<sup>4</sup> for stopping power of molecules. Most of these excitations are expected to give the lowest allowed states, and relatively few excitations are expected in all higher states, since oscillator strengths would indicate such a distribution (30, 31).

The effects of slow secondary electrons are qualitatively different. States which differ in multiplicity from the ground state may also be excited with high probability (35). Since most molecules are in singlet states, this means that triplet state excitations are to be expected. The dissociation of  $H_2$  by such a transition has been verified experimentally by Glockler *et al.* (35, 36) and others.

The lowest excited electronic state of any polyatomic molecule is most likely a triplet state. Much experimental information on these states has been obtained by Lewis, Kasha, McClure, *et al.*, and a summary has been recently given by McClure (37). The theoretical situation has also been investigated quite thoroughly by many authors, Hall (38). Recent calculations have been reported on benzene by Parr, Craig & Ross (39) and on water by Niira (40).

Very little attention seems to have been given the possible role of low triplet state excitations in radiation chemistry, although there are several reasons to believe they may be important. In the first place, they should be

<sup>4</sup> Early work of Bragg *et al.* (32, 33) seemed to indicate that the stopping power of any molecule was the sum of intrinsic contributions from each of its constituent atoms, and that all effects of chemical binding could be ignored. See also Platzman (34).



formed in abundance since their low excitation potentials and high multiplicity favor them over singlet states in slow electron impact. In the second place, they should be relatively effective since their difference in multiplicity from the ground state tends to protect them from destruction by radiation and internal conversion, and thus to preserve them for participation in follow reactions.

*Transfer and migration of electronic excitation.*—The fate of excitation in molecules is one of the most important problems of photochemistry and is discussed in any standard textbook on the subject (41, 42); a recent review by Laidler and Shuler (160) discusses detailed mechanisms. One important property of electronic excitation in a molecule is that it can be transferred. Such transfer can be resonant (to a like molecule) or non-resonant (to an unlike molecule). Non-resonant transfer as a rule involves excitation of vibrational motion and is likely to be irreversible.

Resonant transfer of electronic excitation in condensed systems is known as "exciton migration." The theory of this phenomenon has been presented by Peierls (43), Frenkel (44), Franck & Teller (45) and Wannier (46); its significance in radiation chemistry has recently been discussed by Livingston (47).

Kallman & Furst (48) have recently made an extensive investigation of energy transfer in benzene solutions while under irradiation. Light emission of the solute was used to measure characteristics of the transfer process.

*Dissociation of vibrationally excited states.*—In accordance with the Franck-Condon principle, ionized and excited electronic states of molecules are usually formed with vibrational excitation, frequently with enough excess energy to cause dissociation. What actually happens to such a molecule or ion when it has enough energy to dissociate depends upon competition of all processes which can occur: i.e., dissociation, transfer of electronic excitation, collisional loss of vibrational energy, radiation of energy, internal conversion. A very simple molecule may dissociate in its first oscillation after excitation, but more commonly a molecule has its excess energy distributed among many degrees of freedom so that considerable rearrangement is necessary before dissociation can occur. Eyring *et al.* (49) have discussed the mechanism of the dissociation process as applied to ions in the mass spectrometer. Since this problem is the same as that of the first order chemical reaction rate constant, such work as that of Marcus (50), Magee (51), and Kimball (52) is also pertinent.

Since considerable time may be necessary for a dissociation process, primary decomposition yields are affected by such conditions as pressure or the physical state (41, 42). In liquid systems, of course, the Franck-Rabinowitch caging effect (53) may prevent separation of a radical pair after formation, and thus ensure primary recombination. It is also known that a radical pair may be formed with sufficiently high energy for it to break through the "cage" with 100 per cent efficiency; Franck & Rabinowitch (53) and Norrish (54) pointed out this possibility, and it has been demon-

strated experimentally by Hamill & Schuler (55) in the case of methyl iodide photolysis. Fragments of molecules with considerable excess energy, frequently called "hot radicals," are now believed to be of common occurrence in photochemistry and radiation chemistry. A review of hot radical reactions has been given by Hamill, Williams, Schwarz & Voiland (56).

*Positive ions.*—Mass spectrometric studies can be quite useful in mechanism studies as pointed out by Viallard & Magat (57), and Gordon & Burton (58). However, conditions of ion formation in the mass spectrometer are different from those of ordinary irradiations and so the same ion patterns are not expected in both cases. In particular, collisions of ions in irradiated systems are expected to change the dissociation processes and allow charge transfer and ion clustering.

In irradiated systems most ionization is done by relatively slow secondary electrons which are only able to remove valence electrons. The extent of ionization of the inner shells by primary particles has been considered by Platzman (20) for the case of water and found to be relatively unimportant. However, since Auger showers are expected to occur after inner shell ionization, important specific effects may result, particularly if heavy atoms are present (20).

The theory of charge transfer between monatomic gaseous ions has been given by Holstein (59). Charge transfer in more complicated systems has been discussed by Magee (60) and investigated experimentally by Muschlitz & Simons (61).

Bloom & Margenau (62) have studied cluster formation by rare gas ions. Burton & Magee (63) have pointed out that the clustering tendency in all polyatomic gases should be very great, since the formation process is expected to be bimolecular (instead of termolecular as for rare gas ions). The size of clusters is limited by binding energy and steric effects; one to six attached molecules apparently are possible (62, 64).

*Electron capture.*—It is important to know whether the neutral molecules of an irradiated medium can compete effectively with the positive ions in electron capture because such competition determines the mechanism of the neutralization reaction. In gas phase reactions, the formation of negative ions frequently increases radiolysis yields, as Essex *et al.* (65) have shown. Magee & Burton (66) have made a theoretical study of this problem and reached the conclusion that a low threshold energy for capture (i.e. not appreciably higher than  $kT$ ) is necessary for neutral molecules to capture electrons in competition with ions.

Very little is actually known in detail of the ionization and electron capture processes in condensed molecular media. In liquid water, for example, it has been widely believed that the processes



occurred on exposure to radiation. In this sequence, the ionized electron is supposed to be captured in a water molecule at a considerable distance from the  $\text{H}_2\text{O}^+$  ion. Most of the observed effects of irradiation of water have indeed been quite satisfactorily explained as the action of H and OH radicals. In a recent more detailed examination, however, Samuel & Magee (67) have shown reason to doubt that this particular reaction sequence is responsible for the radicals. These authors have shown that a consistent geometrical description of the subsequent radical reactions in water (as described below in section on Chemical Reaction Mechanism Studies) is possible only if the radicals are formed much closer together than had previously been supposed; in fact, this quantitative description essentially requires a recapture of electrons in their parent ions. Samuel and Magee have used a rough classical model for treatment of the electron escape process and shown that an electron leaving an  $\text{H}_2\text{O}^+$  ion with too little energy to cause additional ionization can very likely dissipate its excess energy in excitation of molecular vibrations before it escapes from the field of its parent ion. A highly excited  $\text{H}_2\text{O}$  molecule will be formed as the electron is recaptured and presumably it will dissociate to form a radical pair ( $\text{H} + \text{OH}$ ).<sup>5</sup>

The work of Samuel and Magee, although not conclusive, casts doubt on the persistence of free positive ions and electrons in irradiated molecular liquids for times sufficient for solvation, and suggests that in such systems they play no role in actual chemical processes. This point of view seems to be in agreement with conductivity work of Taylor (68) and Gerritsen (101).

*Negative ions.*—A book by Massey (69) provides much information on negative ions of atoms and molecules, their structure and formation processes. The recently started work on mass spectrometry of negative ions by Craggs, McDowell & Warren (70), Ahearn & Hannay (71), and others, promises to be valuable for radiation chemistry.

*Charge neutralization.*—A recent review of gaseous ionic recombination reactions has been given by Massey (72). In electron capture by a polyatomic ion  $\text{A}^+$ , an excited state of the molecule A results (73). It may, of course, dissociate immediately. If the ion  $\text{A}^+$  is neutralized in reaction with a negative ion  $\text{B}^-$  (atomic or polyatomic), the author (74) has shown that the most

<sup>5</sup> Platzman has informed the author privately that a more sophisticated theoretical treatment of the electron escape process in water corroborates the earlier belief that the electron can escape to great distances. On the other hand, Allen (94) concluded from a study of experimental data that the H and OH radicals must be formed very close together, and the quantitative study of Samuel and Magee has shown that a consistent picture which involves only radical diffusion requires that pairs of H and OH radicals be formed within several angstroms. The older view, as supported by Platzman's calculation, requires additional mechanisms for the formation of radicals and/or products. Possibilities for a more complicated nature of the initial reactions have been suggested by Haïssinsky & Magat *et al.* (118, 119), Dainton (112) and Stein (120), but detailed model studies have not been made to see whether consistent descriptions of the radiolysis of water can be obtained. Further work is clearly indicated.

likely products are excited states of A and/or B, in preference to any products of metathesis which may be energetically possible.

*Ratio of energy in excitation and ionization.*—The distribution of energy between electronic excitation and ionization is known for many gaseous systems, and there is a remarkable constancy of the energy required to form an ion pair ( $\approx 30\text{--}35$  ev) regardless of the chemical nature of the gas (29). This means, of course, that quite a different fraction of energy must go into excitations from one case to another. Fano (29) has pointed out that systems with low ionization potentials are expected to absorb relatively more energy in excitations, a fact which explains qualitatively the tendency to balance out the net expense of an ion pair. Earlier theories of Bethe (28) and Bagge (75), although very successful in predicting the magnitude of the energy required to produce an ion pair, did not predict an independence of ionization potential.<sup>6</sup>

Slow electrons are relatively more effective than fast particles in excitation of molecular vibrations. In collisions with such simple molecules as  $\text{H}_2$ ,  $\text{O}_2$ ,  $\text{H}_2\text{O}$ , etc. an electron with one to five ev kinetic energy will lose from 2 to 5 per cent of its energy per collision (76, 77). In molecular media part of the expense of an ion pair is attributable to this effect, and it may amount to several electron volts per ion pair.

In liquids, nothing is known about the distribution of energy between excitation and ionization. If the point of view expressed by Samuel & Magee (67) is correct, the question itself has little significance for radiation chemistry.

*Radical reactions.*—The behavior of radicals has been investigated in several branches of chemistry for some years. Monographs by Steacie (78) and Waters (79) are available in addition to the standard works on kinetics (80, 81) and photochemistry (41, 42).

*Isomeric states of molecules.*—Possible effects attributable to isomeric states of molecules seem to have been overlooked in radiation chemistry. By isomeric state we mean an unusual (stable) molecular configuration of higher potential energy than the ground state. A systematic study of this topic has not been made, so this discussion is limited to the mention of two examples.

A linear isomeric state of the  $\text{H}_2\text{O}$  molecule exists ( $^3\pi$ ) according to calculation by Niira (40). This isomeric state can be formed by slow electron impact followed by rearrangement; it has an energy about 2 ev higher than the ground state. Many reactions with radicals ( $\text{H}$ ,  $\text{OH}$ ,  $\text{HO}_2$ , etc.) and solute molecules should be possible for this isomer.

A nonplanar isomeric state (also triplet) exists for ethylene. Mulliken

<sup>6</sup> Platzman has informed the author privately that revised values of ion pair yields in rare gases obtained by Jesse *et al.* (preliminary report in reference (158)) do indeed show a correlation with ionization potential as predicted by Bethe and Bagge. There is apparently a great sensitivity of these measurements to trace impurities.

(82) first remarked on this state and Magee, Shand & Eyring (83) attempted to show that it was involved in cis-trans isomerization reactions. Presumably, it can be obtained by electron impact. This particular isomeric state exists for all ethylenic double bonds and has been postulated as initiator of polymerization reactions (84).

*Tabular summary for elementary processes.*—Table I presents a summary of some of the more important elementary processes from the point of view adopted here.

#### THE FREE ELECTRON SPECTRUM

Fano (85) has recently reviewed the recoil electron energy spectrum. It is generally believed that the theory of Bethe (28, 86) is adequate for the description of recoil electrons from fast primary particles. On the other hand, the distribution of recoil electron energies attributable to slowly moving particles, both heavy particles and electrons, is not as well known (27, 34). Since most ionization is usually attributable to low-energy electrons, the complete free electron spectrum cannot be described in detail.

In radiation chemistry it is the spectrum of all electron impacts to which molecules are subjected which is of most interest, because this will determine the extent to which the various molecular states are excited—for example, low triplet states. Magee & Burton (66) suggested an explicit form for this spectrum which may be satisfactory for approximate consideration.

#### GEOMETRY OF PARTICLE TRACKS

It is convenient to think of the detailed structure of a track as formed in two stages, by the primary and secondary impact processes, respectively. The primary events determine the over-all track density and the secondary events determine the track fine-structure.

It is generally believed that Bethe's theory (28, 86) applied by Williams (87), Lea (15) and others is satisfactory for description of the primary events. Bohr (88) has recently reviewed this theory. Platzman (34) has considered effects of molecular binding and physical state.

Detailed structure of tracks attributable to secondary electrons is not as well understood. It is known that secondary electrons lose their energy quickly, but the space distribution of initially excited and ionized molecules is almost completely unknown. Here the effects of chemical binding must be very important.

The geometry of particle tracks has been discussed by Williams (87), Kara-Michailova & Lea (89), Lea (90), Gray (91, 92), Allen (93, 94), Morrison (95), and Samuel & Magee (67). In spite of uncertainties in detail, rather reliable pictures of tracks can be obtained. Impacting electrons, with energies greater than 100 kev or so, have primary events so widely spaced that they are essentially isolated from each other: almost all recoil electrons lose their energies in distances extremely small compared with interprimary event spacing. Irradiation with high energy electrons,  $\gamma$ - and x-rays, therefore has

TABLE I  
SUMMARY OF ELEMENTARY PROCESSES†

1. Impact processes (primary and secondary particles)	
a. $M \rightsquigarrow M^+ + e$	
b. $M \rightsquigarrow M^*$	Singlet and triplet excitation.
c. $e + M \rightarrow M^-$	
2. Reactions of vibrationally excited ions, molecules‡	
a. $M^+ \rightarrow R_i^+ + R_j$	Various products are possible.
b. $M^- \rightarrow R_i^- + R_j$	Various products are possible.
c. $M^* \rightarrow M'(^*)$	Rearrangement, with or without quenching. May be isomer, or "isomeric state."
d. $M^* \rightarrow A + B$	Ultimate molecule formation.
e. $M^* \rightarrow R_i(^*) + R_j(^*)$	Radical formation, excitation may remain.
f. $M^* \rightarrow R_i^+ + R_j^-$	Ionic decomposition.
3. Reactions producing additional electrons	
a. $M^+ \rightarrow M^{z+} + (z-1)e$	Auger effect.
b. $M^* \rightarrow M^+ + e$	Auto ionization.
c. $M^* + X \rightarrow M + X^+ + e$	Collision ionization.
4. Reactions exchanging charge and excitation	
a. $M^+ + M \rightarrow M + M^+$	Resonant transfer; permits charge migration in condenser phase.
b. $M^+ + X \rightarrow M + X^+$	Nonresonant transfer.
c. $M^+ + X \rightarrow Y^+ + Z$	Transfer with reaction.
d. $M^+ + nX \rightarrow M^+ X_n$	Clustering reaction.
e. $M^* + M \rightarrow M + M^*$	Resonant transfer; exciton migration in condensed phase.
f. $M^* + X \rightarrow M + Z^*$	Non-resonant transfer.
5. Neutralization reactions	
a. $e + M^+ \rightarrow M^*$	Radiative capture is relatively improbable.
b. $M^+ + X^- \rightarrow M(^*) + X(^*)$	One or both may be excited.
6. Radical reactions§	
a. $R_i + M \rightarrow X + R_j$	Radical may be either "hot" or thermal.
b. $R_i + M \rightarrow R_j$	Propagation reaction of polymerization.
c. $R_i + R_j \rightarrow Y$	Radical combination.

† Notation in Table: M, X, Y, Z, A, B represent arbitrary molecules;  $R_i$ ,  $R_j$  represent radicals, atoms; asterisk indicates electronic excitation.

‡ Physical processes, such as collisional deactivation and radiation of energy are omitted.

§ Thermalization of "hot" radical could be listed as a separate process.



the effect of the formation of essentially independent primary events at random throughout a system. The region in which the energy from one of these events is dissipated is compact in a condensed system and can be taken as spherical; we call such a region a "spur."<sup>7</sup> Distribution of spur sizes have been given (89, 67). It should be noted that a significant, but small number of relatively energetic secondary electrons, " $\delta$ -rays," form tracks which cannot be taken as spherical. To a first approximation in radiation chemistry their special effects can be neglected, since they are also isolated from other portions of the track.

Relatively slower primary particles, such as Mev  $\alpha$ -particles, produce primary events which have a smaller spacing than secondary electron ranges. A continuous cylindrical track is, therefore, obtained. Of course " $\delta$ -rays" produce small branching tracks.

Tracks of low-energy  $\beta$ -particles (tritium  $\beta$  for example) are intermediate in character between high-energy electrons and heavy particles. At first they consist of independent regions which rather quickly merge to form a continuous track.

#### TIME SCALE FOR RADIATION CHEMISTRY

From a chemical point of view, impact processes (i.e., ionization and excitation) both by primary particles and secondary electrons, and initial molecular dissociation are essentially instantaneous. All other processes involve molecular collisions and take place on a much longer time scale. Morrison (95) has recently given a brief discussion of the time scale of events.

In the condensed state, the pattern of primary and secondary ionization and excitation is established in less time than it takes a molecule to dissociate. An average secondary electron has, say, 75 ev and its energy is reduced below the lowest excitation potential of the medium ( $\approx 5$  ev) in about ten collisions which will take little more than  $10^{-15}$  sec. At this time there are several electrons in the same vicinity, all with energies less than the excitation potential of the medium. If the point of view expressed by Samuel & Magee (67) is valid, these electrons will be trapped with their parent ions in about  $10^{-13}$  sec. All of this takes place before the dipole orientation part of the dielectric constant can relax (96, 97).

The high electronic excitation of such a region caused by one recoil electron from the primary particle (which we call a "spur") gives rise to radical formation. Radicals formed in such proximity have a chance to react with each other before they can diffuse away. For a spur, this initial reaction takes place in about  $10^{-8}$  sec. as calculated from the model of Samuel & Magee (67), after which, the escaped radicals have a greater chance of reaction with molecules or radicals in the system at large. All other chemical reactions, such as reaction of radicals with solutes, etc., take place more slowly.

<sup>7</sup> The term "cluster" has sometimes been used. Since "cluster" is applied to the unrelated aggregation of neutral molecules about ions in the gas phase, we prefer to use a different expression here.

For the sake of orientation, Table II summarizes a time schedule for some typical events which are of interest in radiation chemistry. These times are to be taken as approximate and suggestive rather than as exact, well-known quantities.

#### DYNAMICS OF PARTICLE TRACKS

A system exposed to steady irradiation has concentrations of intermediates which vary both in space and time. High concentrations are produced locally with each track; at any time there are randomly spaced tracks of various ages, and at any point there is a time variation of the intermediate concentrations as various tracks cross the point. It is the problem of radiation chemistry to describe the chemical reactions in such a system.

Dainton (98) and others have called attention to these aspects of radiation chemistry. The author (99) set up a model, applicable for cylindrical tracks, in which a periodic behavior of concentrations of intermediates at any point was visualized. Account was taken of the fact that intermediates from previous tracks have not entirely disappeared when a new track is formed, i.e. a "background" of intermediates exists in such a system. "High background" and "low background" cases exist. Of course, track effects are most pronounced in low background systems, i.e., when tracks essentially dissipate as isolated events. In condensed systems this case is always expected for moderate irradiation rates. In contrast, the high background case means that a single track adds very little extra to intermediate concentration, and there is essentially a uniform spatial distribution in spite of the track mechanism for their formation. Radiolysis of gaseous HBr, discussed above, is an example of this case.

Many discussions of the dynamical aspects of particle tracks have been given. A cylindrical track model for ionic recombination was originally used by Jaffe (100) and later re-examined by Zanzstra (161), by Kramers (159), and by Gerritsen (101). Lea (15) used it for diffusion and recombination of radicals in water. Geometrical considerations above have made it clear that such a model is inadequate for irradiation with electrons, x- and  $\gamma$ -rays; Kara-Michailova & Lea (89) attempted to improve the model by introducing spurs explicitly into a treatment of gas phase ionic recombination. Allen (94) has more recently discussed the spur mechanism of radical formation and reactions in water. Tobias (102) has considered dynamic aspects of the biological action of radiation. Samuel & Magee (67) have made a study of the radiolysis of water using a detailed model for diffusion and reaction of radicals in spurs. These authors made calculations for irradiations with  $\gamma$ -,  $\alpha$ - and tritium  $\beta$ -rays; satisfactory agreement with experimental results was obtained (see below). Toulis (103, 104) has studied effects of ionization density of primary particle in water radiolysis.

For much of radiation chemistry it has been a truism that initial yields ( $G$  values) are independent of dose rate (105). This result, of course, is understood on the basis of the independence of the individual tracks ("low back-

TABLE II  
APPROXIMATE TIME SCALE FOR RADIATION CHEMISTRY

Time, sec.	Events
$10^{-18}$	Primary electron (Mev) traverses molecule.
$10^{-17}$	Mev $\alpha$ -particle traverses molecule.
$10^{-16}$	Secondary electron (5 ev) traverses molecule.
$10^{-15}$	Thermal electron (0.025 ev) traverses molecule.
$10^{-14}$	Molecular vibration. Fast molecular dissociation.
$10^{-13}$	Electron capture in molecular liquid.
$10^{-12}$	Radical moves one jump in diffusion.
$10^{-11}$	Dielectric relaxes, liquid. Collision time, thermal electrons in gas
$10^{-10}$	(1 atm pressure).
	Collision time, molecules in gas (1 atm pressure).
$10^{-9}$	Secondary electron (5 ev) thermalized† in gas (1 atm).
$10^{-8}$	Lifetime for radiation of excited singlet state (allowed).
	Forward reaction complete in $\gamma$ -ray "spur" in water.‡
$10^{-7}$	Thermal electron captured§ in gas.
	Forward reaction completed in $\alpha$ -ray track in water.‡
$10^{-6}$	
$10^{-5}$	
$10^{-4}$	Reaction time for radical without solute in molar concentration.‡
$10^{-3}$	
$10^{-2}$	Lifetime for radiation of triplet state.

† Assumption is made that 2 per cent of its energy is lost per collision.

‡ For definition of forward reaction see section on radical reactions in water, below. Time calculation according to reference 67.

§ Assumption is made that capture probability per collision is  $10^{-3}$ .

# Assumption is made that specific reaction rate constant is  $10^{-16}$  cm<sup>3</sup> (molecule sec)<sup>-1</sup>. This corresponds to approximately 5 kcal/mole activation energy.

ground" case). Dainton (106) came to this conclusion in studies of irradiation-induced polymerization. It is doubtful that track overlap effects could be obtained with steady irradiation without introducing extraneous effects of heating. Intermittent irradiation may furnish a means for such investigation.

### EXPERIMENTAL RESULTS

No up-to-date summary of experimental results is available. Lind (14) reports all results available in 1928. Lea (15) presents tables of typical gas and solution reactions. Summaries of selected recent work in aqueous solution are given by Miller & Wilkinson (107), Hardwick (108), and Lefort (109). A bibliography of papers on the effects of  $\alpha$ -,  $\beta$ -,  $\gamma$ - and x-rays on organic compounds has been prepared by Sachs (110).

### CHEMICAL REACTION MECHANISM STUDIES

A complete mechanism would account for the formation and disappearance of all transient intermediates. In a given case, a partial mechanism which accounts for the principal observations is first constructed. "Fine-structure" studies are then made by the isolation of individual steps to give more detail. As in chemical kinetics, a mechanism is never accepted as complete, but, nevertheless, tentative mechanisms have always been extremely valuable.

It is natural to divide a mechanism into two parts: (a) one describes the behavior of the long lived (radical and molecular) intermediates; (b) the other describes the electronic conditions which lead to the radical formation. This order, which may appear to be inverted, is more natural from a chemical point of view, since from chemical evidence it is usually known what radical intermediates had to be present in a particular case.

*The radical reactions in water.*—A rather large fraction of radiation chemistry has been concerned with studies of water and aqueous solutions, to a large extent because of the unique importance of water, particularly in biological systems. A good summary of the present status of the radiation chemistry of pure water has been given by Allen (94). Important work on water has been reported by Weiss (111), Allen (93, 94), Dainton (112), Allen, Hochanadel, Ghormley & Davis (113), Hochanadel (114), Bonet-Maury (115), Johnson & Allen (116), Hart (117), Toulis (104), and Lefort (109).

The products of radiolysis of pure water are  $H_2$ ,  $O_2$  and  $H_2O_2$  in yields which vary with the irradiation conditions. Much of the experimental data can be explained if it is assumed simply that irradiation induces the following two reactions in water (113, 114, 117):<sup>8</sup>



<sup>8</sup> The possibility for a more complicated nature of the initial reactions in water has been emphasized by Haïssinsky (118), and Haïssinsky & Magat (119), Dainton (112), and Stein (120).

The formation of these products is tacitly assumed to be homogeneous in space, and thus all the details of track geometry are ignored in this mechanism. The yields ( $G$  values) of these primary reactions do, however, depend upon the irradiation conditions, principally the ionization density of the radiation.

This simple treatment of the primary process is not in disagreement with the geometry and dynamical behavior of tracks discussed above. The  $F$  reaction, of course, is accounted for by the "initial" radical combination and the  $R$  reaction by the radicals which escape initial reaction. In Table III, some experimental values are compared with calculated values of radical yields. It should be emphasized that this calculation was not completely *a priori*, but that the size of the "spurs" was taken somewhat arbitrarily in order to obtain good agreement for  $\gamma$ -irradiation.<sup>9</sup> It does appear, however, that the principal features of water radiolysis can be understood in terms of these radical effects.

TABLE III  
FRACTION OF DETECTABLE† RADICALS ENTERING FORWARD REACTION

Type of Radiation	Experimental‡	Comments	Calculated (67)
Gamma rays, x-rays	0.21	Hart (117) HCOOH solution	0.23
	0.25	Hochanadel (114) KBr solution	
	0.22	Johnson (121) Acid FeSO <sub>4</sub> solutions	
Tritium beta rays	0.30	Hart (117) HCOOH solution	0.31
Alpha rays	0.90	Hart (122) HCOOH solution	~0.89
	0.90	Allen (123)	

† Radicals which combine to product H<sub>2</sub>O are undetected.

‡ This value is  $G_F/(G_F + G_R)$ .

*The ferrous sulfate reaction.*—In the radiation chemistry of aqueous solutions the oxidation of ferrous sulfate has held a rather unique position. It has been investigated often, and although it has frequently been used as a dosimeter, its mechanism and yield are both still in dispute. Reported  $G$  values are conveniently summarized by Miller & Wilkinson (107) and Hardwick (108).

The earliest investigation was made by Fricke & Hart (124). More recent work has been reported by Todd & Whitcher (125), Miller & Wilkinson (107) and Miller (126), Hochanadel (127), Hart (128), Hardwick (129), Riggs, Stein & Weiss (130), Amphlett (131), Dewhurst (132), Johnson (121),

<sup>9</sup> See discussion of electron capture in section on Elementary Processes.

Hummel & Spinks (133), and others. Values of the yield as a function of dose, pH and the concentration of various solutes ( $\text{Fe}^{++}$ ,  $\text{Fe}^{+++}$ ,  $\text{O}_2$ ,  $\text{H}_2$ ,  $\text{CO}_2$ ,  $\text{F}^-$ ,  $\text{SO}_4^-$ , organic compounds) have been reported. Reported  $G$  values range from 15.5 (127) to 20.8 (126).

*Statistical nature of processes.*—In view of the potentially complicated nature of radiation effects it is natural to look for possible simplification of interpretation. A picture of completely nonselective action is a reasonable limiting case to consider. Studies of product distribution in radiolysis of saturated aliphatic hydrocarbons and their acids by Whitehead, Goodman & Breger (134) and Breger (135) have supported this point of view. It is found, for example, that the ratio of  $\text{H}_2$  yield to  $\text{CH}_4$  yield in the radiolysis of a number of different hydrocarbons is proportional to the ratio of the number of C—H bonds to the number of C— $\text{CH}_3$  bonds, and Burton (2) has stated a statistical principle: "Where special chemical effects can be neglected, nature and quantity of the products are determined by nature and number of parent groups in the molecule of the substance decomposed."

Although there is usually reason to suspect that chemical effects cannot be ignored, this principle is useful as a sort of ideal behavior for a substance. As a result of the rather important role of secondary electrons in impact processes and negative ion formation, both of which have marked selective nature, it is expected that selectivity should appear at an early stage.

In the radiolysis of pure compounds exceptions to statistical behavior are easily found. The most well-known example is the great stability of aromatic compounds (136); in mixed aliphatic-aromatic compounds such as toluene and ethyl benzene, the aliphatic part is preferentially decomposed (137, 138). Gevantman & Williams (139) have shown that in radiolysis of alkyl halides, the carbon-halogen bond is broken most often.

In the radiolysis of mixtures of compounds, many selective features should be apparent from theoretical considerations. Thus, (a) Secondary electron impact processes: the mixture component with lowest ionization potential should form relatively more positive ions; the component with lowest excitation potential will form relatively more excited states. (b) Electron capture processes: those components which are able to capture electrons will compete for the slow electrons. (c) Transfer of charge and excitation: there will be a tendency for the components with the lowest excitation and ionization potentials to take all of the excitation and charge. Since a relatively long time is available, this transfer can be complete, even to a small component. (d) Radical formation processes: a component's ability to form radicals will depend upon its ability to keep its charge or excitation and dissociate in competition with collisional deactivation, etc. (e) Radical reactions: components compete with each other in the radical reactions.

These considerations emphasize the importance of the study of binary systems, particularly of pairs of compounds which differ only slightly in properties, as a means to isolate steps in the radiolysis mechanism. Gordon & Burton (58), Manion & Burton (138), and Patrick & Burton (140) have made such studies.



*Protection and sensitization.*—In a mixture each component is either protected or sensitized by the others because of the effects listed above. The importance of protection and sensitization has long been realized, particularly in connection with biological systems. The role of charge and excitation transfer has been studied by Burton *et al.* (138, 140, 141). Protection in radical reactions has been investigated in gas phase work by Mund, Huyskens & Lories (142), and in aqueous solute reactions by Dale (143). Extensive work has been done in biological systems, and here we can only call attention to a recent review article by Patt (144), and to papers by Latarjet, Hollaender, Zirkle, and Dale in reference 8.

*Use of electric field.*—Essex *et al.* (65) have used an applied electric field for the isolation of various steps in gas phase reactions. They have studied the role of positive-negative ion neutralization, electron capture, and excitation by slow electrons. It is found, generally, that as free electrons are able to gain more energy from the applied field (by increasing the ratio field strength to pressure) *G* values of radiolysis usually increase. It is possible to separate electron capture and excitation effects. This work is now being continued by Professor Burt at Syracuse.

A radio frequency technique has been used with great success in studies of electron-ion recombination and electron capture in gases by Biondi (145), and Holt *et al.* (145, 146). This technique could be applied profitably in radiation chemistry.

*Intermittent irradiation studies.*—Under conditions of steady irradiation, transient intermediate concentrations build up to a steady value which then determines the rate of reaction. Studies of transient conditions have been used in photochemistry by Burns & Dainton (147) to determine reaction rate constants of radical reactions. This technique has recently been applied in radiation chemistry by Hart & Matheson (148). The intermittent radiation can be obtained by means of a rotating disc with sectors which alternately transmit and block radiation; consequently, this technique is sometimes called the "sector method." Hardwick (105) used pulsed radiation from an x-ray tube in similar studies.

*Use of stable isotopes.*—Stable isotopes, particularly deuterium and oxygen, have been useful in mechanism studies. As examples, work in gas phase by Mund *et al.* (142, 149), in organic mixtures by Gordon & Burton (58) Patrick & Burton (140), and aqueous solution by Hart (117) can be mentioned.

*Use of radioactive isotopes.*—Radioiodine has been used by Gevantman & Williams (139) in studies of the spectrum of radicals formed in radiolysis of alkanes and alkyl iodides. Since iodine is a "scavenger" (i.e. it reacts rapidly and indiscriminantly with all radicals), it is possible to "tag" all radicals produced. These studies have brought to light many dissociations and rearrangements previously unsuspected.

Other work in radiation chemistry with "tracers" has been carried out by Schuler & Hamill (150) and Zubler, Hamill & Williams (24).

Radioisotopes have, of course, also been added to chemical systems as

sources of  $\alpha$ -radiation (14, 151) and  $\beta$ -radiation (108, 117, 129, 152).

*Use of chemical scavengers.*—Chemical compounds which are "scavengers" have been used to react with radicals for various purposes. Magat *et al.* (153) have used DPPH (di-phenyl picrylhydrazyl) in organic liquids to determine the total number of radicals produced in radiolysis, and they find  $G$  values from 1 in carbon disulfide to 70 in carbon tetrachloride. This method yields valuable results regarding radiation stability of compounds, but complications arise regarding interpretation of results, as pointed out by Wild (154).

Polymerization has also been used to scavenge free radicals (153, 106, 155, 156, 157).

*Temperature studies.*—Chemical reactions, diffusion processes, etc. always have temperature dependent rates. In complicated systems such as are frequently found in radiation chemistry there may not be a simple interpretation to the temperature coefficient of the over-all effect. A tentative mechanism, however, suggests a temperature dependence, so that such studies are always useful. Hamill, *et al.* (56) have pointed out this technique for the isolation of "hot radical" steps in a mechanism.

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# CHEMICAL EFFECTS OF NUCLEAR TRANSFORMATIONS<sup>1</sup>

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## INTRODUCTION

All nuclear transformations yield product atoms which initially have abnormally high kinetic energy or electrical charge or both. The kinetic energy is acquired as a result of the requirement of conservation of momentum in the capture or emission of a particle or photon. Charge may result from negatron, positron or  $\alpha$ -particle emission, and also from electron capture, internal conversion and Auger electron (1) emission.

For example, a  $\text{Br}^{82}$  atom which has just been formed by the  $\text{Br}^{81}(n, \gamma)\text{Br}^{82}$  reaction with the emission of a 7 Mev  $\gamma$ -ray will have a recoil energy of 322 ev. or about 7400 kcal./mole, while an  $\text{S}^{35}$  atom formed by emission of a 0.59 Mev proton in the  $\text{Cl}^{35}(n, p)\text{S}^{35}$  process is born with an energy of some 16,400 ev.  $\text{Br}^{80}$  produced by the isomeric transition of  $\text{Br}^{80m}$  has a minimum charge of plus 1 and an average charge of plus 10.

Since chemical bond energies are rarely in excess of 5 ev, the recoil energies and charges resulting from many nuclear processes are sufficient to rupture the parent bond of the atom, and allow it to break many bonds in neighboring molecules, before being slowed to thermal energies.

The fraction of starting materials converted to products in studies of such activation by nuclear processes is usually so small that no change in the composition of the medium can be detected by chemical means. The products may, however, be identified by their radioactivity after separation with the aid of specific carriers or chemical procedures. With a knowledge of the product species, there is a possibility of deducing the nature of the bond rupture processes by which the highly activated atoms lose their energy and finally achieve new stable chemical combination. Two criteria which must be met in this type of investigation are that the nuclear process produce a radioactive product and that the stable molecules which are formed by the product atoms shall not undergo thermal exchange with each other or with the parent molecules.

Nuclear transformations offer the kineticist a new method for activating atoms. The energy supplied is usually tremendously in excess of the amount needed. For some purposes this may be an advantage and for others a disadvantage. It has, however, the unique advantage that the particular atom

<sup>1</sup> The survey of the literature pertaining to this review was concluded in March, 1953.

<sup>2</sup> The writing of this chapter was done as part of work related to a research program supported by the Research Committee of the University of Wisconsin and by the United States Atomic Energy Commission.

which is activated is tagged with radioactivity by the same act which activates it. With this label attached, this particular atom can be identified in the reaction products.

The majority of more than a hundred studies which have been made in this field since its discovery by Szilard & Chalmers (2) in the year 1934 have used activation by radiative neutron capture. This is due to the relative availability of neutrons; the relative ease of using them under conditions where radiation damage and temperature effects are not serious; favorable capture cross sections for the  $(n, \gamma)$  process; and the fact that the  $(n, \gamma)$  process is capable of producing a number of radioactive species with chemical properties which are particularly suitable for studies of this type.

Several good surveys of different aspects of this field have been published. For example, Libby (3) and Edwards & Davies (4) have discussed the nuclear processes which may lead to activation and have developed the equations for calculation of the energy of the product atom. In the book edited by Wahl & Bonner (5), Barnes, Burgus, & Miskel have reviewed the field and tabulated references to experimental work available by the end of 1949. Other reviews include those by Williams (6), Maddock (7), McKay (8), Broda (9), and Green (10).

The purpose of the present chapter is to survey and correlate some of the most significant recent work. It will not cite all the literature published since the earlier reviews, but will summarize some of the results which at the moment seem most useful in extending an understanding of the field and suggesting experiments.

*Terminology.*—Because of the high excitation energies involved, research in this field is frequently called "hot atom chemistry." The term is, however, somewhat ambiguous. Chemists in other fields often assume that it is a colloquial expression synonymous with "radiochemistry." On the other hand there is possibility of confusion with the terms "hot atom" and "hot radical" as used in photochemistry. This has become more true in the light of recent evidence that the chemical transformations caused by nuclear processes may result from a combination of reactions of highly energetic atoms and reactions of thermalized atoms. There is some tendency for authors to be more explicit by using such terms as "chemical effects of nuclear transformations" and "activation by radiative neutron capture."

In this chapter the term "high-energy process" will be used to designate any reaction by which an atom activated by a nuclear process enters stable molecular combination before it has had opportunity to exist in thermal equilibrium with the medium. Processes by which such atoms enter combination after undergoing collisions in thermal equilibrium with the medium will be called "thermal processes." High-energy processes will include reactions of the type  $C_2H_5 + Br \rightarrow C_2H_5Br$  where the atom combines with a radical it has formed in losing its excess energy, before escaping from the solvent cage in which the fragmentation occurred. It will also include "hot" reactions of the type observed in photochemistry and "epithermal reactions" as defined by Libby & co-workers.

The terms "organic yield," and "inorganic yield" will be used frequently as meaning the ratio of the number of activated atoms which enter organic combination or inorganic combination, to the total number of activated atoms.

### PHYSICAL PROCESSES

*$\gamma$ -ray spectra from ( $n, \gamma$ ) processes.*—Partial  $\gamma$ -ray spectra from radiative neutron capture by some 35 elements have now been determined. The  $\gamma$ -rays were produced by allowing a beam of thermal neutrons from a nuclear reactor to fall on a sample of the target substance. Their energy was measured either: (a) by measurement of the length of proton recoil tracks from the  $D(\gamma, n)H$  reaction in photographic plates soaked in  $D_2O$  [Hamermesh (11)]; (b) by a coincidence pair spectrometer [Kinsey, Bartholemew & Walker (12)]; or (c) by a scintillation spectrometer [Hamermesh & Hummel (13, 14)]. In every case the spectrum is complex. The average number of  $\gamma$ -rays emitted as a result of the ( $n, \gamma$ ) process in the elements from  $_{11}Na$  to  $_{72}Hf$  varied from about two to six, and was independent of neutron energy at least in the low-energy region [Muehlhause (15)]. No evidence was found for angular correlation.

The data on  $\gamma$ -ray spectra are insufficient to allow calculation of average recoil energies for any ( $n, \gamma$ ) process. An idea of the possible contribution of cancellation effects is given, however, by Cobble & Boyd (16) who have calculated that the portion of the atoms which receive less than 10 eV recoil energy from the  $Br^{81}(n, \gamma)Br^{82}$  reaction will be about 5, 3, and 1.5 per cent for the emission of 6, 4, and 3  $\gamma$ -rays respectively. If the time between emission of consecutive  $\gamma$ -rays is greater than the time required for an atom to move about one atomic diameter (about  $10^{-14}$  sec.), the atom may however break its parent bond and adjacent bonds as the result of the separate recoil impulses from the successive  $\gamma$ -rays even in the case where there would have been complete cancellation of momentum if the  $\gamma$ -rays had been emitted simultaneously. Lifetimes of the intermediate levels in the  $\gamma$ -ray cascade processes of interest for this work probably vary from  $10^{-17}$  sec. to much longer than the critical time of  $10^{-14}$  sec. (17). From the calculations cited (16) and from a number of investigations which show that radiative neutron capture leads to rupture of the chemical bonds of the product atom in a high percentage of the events in the gas phase it may be concluded that  $\gamma$ -ray cancellation is relatively unimportant in protecting parent molecules from rupture.

*Internal conversion of capture  $\gamma$ -rays.*—Evidence of internal conversion following radiative neutron capture has now been found with eleven nuclides and none has been tested which did not show the effect. Hibdon & Muehlhause (18) have observed the conversion electrons from neutron capture in  $_{48}Cd^{113}$ ,  $_{62}Sm^{149}$ ,  $_{64}Gd$ ,  $_{66}Dy$ , and  $_{88}Hg$  with a  $180^\circ$   $\beta$ -ray spectrograph. The K/L ratios and energies favor transitions which would range in lifetime from  $10^{-12}$  to  $10^{-9}$  sec. Wexler & Davies (19) have exposed ethyl bromide and ethyl iodide at pressures of about three microns and a neutron flux of  $10^{12}$  neutrons/cm.<sup>2</sup>/sec. in vessels provided with collecting electrodes which allowed

the charged recoil particles to be distinguished from the uncharged by the radioactivity on the electrodes after irradiation. The results indicate that a minimum of 12 per cent of the  $\text{Br}^{80m}$  (4.4 hr.), 25 per cent of the  $\text{Br}^{82}$  (36 hr.), 50 per cent of the  $\text{I}^{128}$  (25 min.), and approximately 18 per cent of the  $\text{Br}^{80}$  (18 min.) was positively charged as a result of internal conversion during stabilization of the compound nucleus following neutron capture. Yosim & Davies (20) have demonstrated that the majority of gold and indium recoil atoms which escape from the surface of gold and indium films during neutron irradiation are positively charged. They have reasoned that the internal conversion process which produces the charge must occur sufficiently later than the emission of the energetic  $\gamma$ -rays to allow the atom to escape from the surface, because if internal conversion occurred in the surface the atom would be neutralized before escaping. Magnusson has also collected gold atoms ejected from a surface by recoil from the  $(n, \gamma)$  process, but has not tested their charge (21).

In view of the above results it now seems probable that chemical effects following radiative neutron capture are attributable, at least in part, to reactions resulting from the neutralization of the charge produced on the atom by internal conversion after it has lost its recoil energy. Several investigators (7, 16, 19, 20, 22, 23, 24) have called attention to this fact.

*Average charge following internal conversion and electron capture.*—The average charge on  $\text{Br}^{80}$  (18 min.) produced by the isomeric transition  $\text{Br}^{80m}$  (4.4 hr.)  $\rightarrow$   $\text{Br}^{80}$  (18 min.) has now been determined by Wexler & Davies (25) to be plus 10, while Miskel & Perlman (26) have shown that the average charge on  $\text{Cl}^{37}$  formed by electron capture in  $\text{A}^{37}$  is plus 4. Both determinations were made by measurement of the current produced by the collection of the primary charged ions from the nuclear process, in a gas at very low pressure, decaying at a known rate. The bromine result is about twice that predicted earlier on the assumption that only one electron was internally converted in each transition event.

## CHEMICAL EFFECTS

### REACTIONS IN LIQUID ORGANIC MEDIA

*Introduction.*—Because of the relatively simple chemical properties of the alkyl halides and because of the favorable nuclear properties of the halogens, investigations of the chemical reactions initiated by neutron capture and by isomeric transition in these compounds have proved to be particularly fruitful. The discovery of phase, structure, "scavenger," and isotope effects are among the significant advances of the last few years which will be outlined below.

*Proposed mechanisms of reactions activated by the  $(n, \gamma)$  process.*—The fact that recoil halogen atoms produced by radiative neutron capture in gaseous alkyl halides are nearly always found in inorganic combination (19, 24, 27, 28, 29, 31, 32) indicates that the efficiency of bond rupture follow-

ing the nuclear process is high. Consequently the organic yields of 20 per cent and more normally observed in liquid phase reactions must result from re-entry of the recoil atom into organic combination. The two hypotheses which have been suggested to rationalize the yield in condensed phases may be termed the "billiard ball collision-epithermal collision" hypothesis and the "random fragmentation," "brush heap," or "nest of radicals" hypothesis.

The billiard ball collision hypothesis postulates that atoms recoiling with a few hundred ev of energy in liquid or solid alkyl halides lose their energy by momentum transfer in elastic collisions with single atoms [Libby (3); Miller, Gryder & Dodson (33a); Capron & Oshima (33b)]. It is assumed that this transfer occurs just as if the atoms were isolated atoms in the gas phase. Thus, for example, an iodine atom which has undergone neutron capture in ethyl iodide is postulated to lose its energy by a series of collisions with the iodine and hydrogen atoms. The fractional energy loss per collision in such cases is  $E_{\text{loss}}/E_{\text{initial}} = [4MM_1/(M + M_1)^2] \cos \theta$  where  $M$  and  $M_1$  are the masses of the impinging atom and the struck atom respectively and  $\theta$  is the angle between the paths of the atoms after collision. A head-on collision with an iodine atom would lead to nearly complete transfer of energy to the struck atom, thus projecting it into the medium. The de-energized impinging atom would remain in the solvent cage with the ethyl radical abandoned by the struck atom and so would have a high probability of combining with it to form a new ethyl iodide molecule. If the collision were glancing rather than head-on, the energy transfer would not be complete and the impinging atom would escape from the cage without undergoing combination with the organic radical.

A head-on collision with a hydrogen atom would result in the loss of only about 3 per cent of the energy of the iodine atom. Since about 4 ev are required to break a C—H bond, the iodine atom would retain 120 ev or so after breaking such a bond and would therefore not be expected to stay in the solvent cage with the radical formed by the bond rupture.

As elaborated to this point, the billiard ball hypothesis would predict that all of those recoil atoms which re-enter organic combination must do so as the parent compound. When it was observed that recoil halogen atoms in dilute solutions of halogen in pure hydrocarbons could enter organic combination [Reid (34)] and that dibromo propanes were formed from irradiation of propyl bromide (35), it was suggested by Friedman & Libby (35) that this might be explained by assuming that when the energy of the recoil atom is reduced to the order of 10 ev by successive collisions with hydrogen atoms a new type of energy transfer becomes possible. It was postulated that in this energy region, but not in the 100 ev region, the halogen atom may transfer energy to molecules as a whole in inelastic collisions, with subsequent rupture of one of the bonds of the molecule resulting from vibrational excitation. If a hydrogen bond were broken in such a process the halogen atom would be in the cage with the radical formed and thus would have an opportunity to substitute for the hydrogen in reforming a stable molecule. Reactions of this



type have been termed "epithermal" reactions in contrast to those occurring at higher energies and resulting from collisions between atoms in the manner described in the preceding paragraph.

The billiard ball collision-epithermal collision hypothesis has been further extended by Friedman & Libby (35) and Fox & Libby (36) to rationalize the fact that the ( $n, \gamma$ ) activated reactions of the propyl bromides in the solid state give different ratios of the different organic products than in the liquid state. It has also been applied to the bromine isotope effect (36, 54).

This hypothesis has played an important role as the dominating hypothesis in its field to date. The fact that various investigators have felt dissatisfaction with it has served to stimulate experimentation. As elucidated and applied thus far, it involves certain oversimplifications and unproved assumptions, and is unable to give a consistent correlation of all the experimental facts. Among the reasons for this conclusion are the following.

I. The assumption that the momentum transfer events which a recoil atom experiences in the liquid or solid phase are identical with those between isolated atoms in the gas phase must be far from correct.

II. It has been demonstrated (22, 23, 37) that a considerable portion of both the organic and inorganic yield from the ( $n, \gamma$ ) process in alkyl bromides and alkyl iodides occurs after the recoil atoms have undergone many collisions subsequent to attainment of thermal equilibrium with the medium. (For a more detailed discussion of this and the following point see section under "scavenger effect.")

III. Experiments show (37) that inorganic as well as organic compounds of the recoil atom may be formed by "high-energy processes" (see section on Terminology). Such a possibility is not considered in the billiard ball-epithermal theory, as developed to date.

IV. The organic yield of some of the alkyl iodides is no greater in the solid phase at  $-196^\circ$  than in the liquid phase at room temperature (22, 31, 37). The billiard ball-epithermal hypothesis predicts that the organic yield should always be higher in the solid phase.

The second of the two hypotheses mentioned at the beginning of this section, the "random fragmentation" hypothesis, is broad enough to rationalize all the observations mentioned above. Its postulates are as follows. When a halogen atom in a liquid phase molecule acquires several hundred ev of recoil energy it starts moving rapidly but having traveled less than a molecular diameter encounters a solvent molecule. If this were an isolated molecule the energetic atom would transfer momentum to it or to one of its atoms in an elastic collision and would continue on its way. In the liquid phase this cannot happen because the struck molecule is backed by and surrounded by a close packed and sometimes intertwined wall of other molecules. The result is that the energy is dissipated by breaking bonds in a rather indiscriminate fashion in the immediate vicinity of the energetic atom. When the energy of the atom has been reduced below bond breaking energies it will find itself in, or adjacent to, a pocket of high local concentration of organic



radicals and inorganic atoms. It may combine with one of these after it has been moderated to an energy where combination is possible but before it has had opportunity to diffuse in the system as a thermal atom. Alternatively it may enter stable combination by a "thermal process," after diffusion in thermal equilibrium with the medium. In a pure alkyl iodide or bromide, where the activation energy for all possible reactions of the halogen atom with the solvent is high, the thermal atom will nearly always combine with a radical or atom which it produced in losing its recoil energy, and which it encounters after varying numbers of collisions with solvent molecules. Such thermal reactions are vulnerable to competition from low concentrations of impurities such as olefins and from added elemental halogen.

The relative numbers and specific types of organic and inorganic fragments formed by the recoil atom must depend on the chemical nature, density, and crystal structure of the medium and on the mass, and possibly the energy of the recoil atom. The relative yields of the recoil atom in different product species will depend, then, on these same factors. It may also depend on the activation energies for its reactions with stable molecules of the medium.

*The "scavenger" effect.*—One of the most revealing techniques to be used in investigating the chemical consequences of the ( $n, \gamma$ ) process in liquid organic halides has been the addition, prior to neutron irradiation, of low concentrations of substances known to react readily with thermalized halogen atoms. Thus 1 mole per cent or less of elemental bromine present in ethyl bromide (37) or of elemental iodine present in various iodides (22, 37) during neutron irradiation reduces the organic yield by 15 per cent or more of its value for the pure liquid, but a further increase in the halogen concentration reduces the yield relatively little. That part of the organic yield which is relatively insensitive to added halogen has been attributed (22, 23, 37, 38) to high-energy processes. That part which is sensitive has been ascribed to thermal processes, usually involving diffusion of the recoil atoms to radicals which they formed in losing their energy. Consequently the fact that the organic yield of ethyl bromide is reduced from 32 per cent to 25 per cent, but no further, by low concentrations of added bromine may be considered to mean that when pure ethyl bromide is irradiated, 25 per cent of the recoil atoms enter organic combination by high-energy processes and 7 per cent by thermal processes. Similarly the fact that the organic yield is raised from 32 per cent to 60 per cent but no higher by 0.1, 0.2, or 1 mole per cent of  $\alpha, \beta$ -dibromoethylene seems to mean that 40 per cent of the recoil atoms enter inorganic combination by high-energy processes and 28 per cent enter inorganic combination by thermal processes (37). The fact that a large fraction of the inorganic yield is attributable to high-energy processes is of particular interest.

The important discovery that  $\alpha, \beta$ -dibromoethylene will react readily with bromine atoms but not with bromine molecules was made by Williams, Hamill, Schwarz & Burell (39, 40). Similarly, using allyl bromide in ethyl

bromide, these investigators added carriers following neutron irradiation and identified the products by chemical fractionation. The results indicated a division of reactions between the high energy and thermal type, similar to that obtained using bromine and  $\alpha,\beta$ -dibromoethylene as scavengers cited in the preceding paragraph. The bromolefins have also been used in other work (29, 41) from the same laboratory to assess the importance of thermal bromine atoms from both neutron capture and isomeric transition reactions.

On the basis of the hypothesis proposed to explain the sensitivity of the organic yields of bromides and iodides (22, 37) to free halogen scavengers it was predicted (37) that there would be no scavenger effect in alkyl chlorides because the ease with which chlorine atoms react with carbon-hydrogen bonds to form stable hydrogen chloride would preclude their existence as atoms in thermal equilibrium with the medium. The prediction has been confirmed, by experiments on nine different alkyl chlorides (31), as has the corollary prediction that there should be a scavenger effect with carbon tetrachloride (31, 42)

*Effect of molecular structure.*—The organic yields of the  $I^{127}(n, \gamma)I^{128}$  reaction in eight liquid iodides (22) fall into three distinct groups: (a) about 60 per cent for  $CH_3I$  and  $CH_2I_2$ ; (b) about 41 per cent for the primary iodides higher than methyl ( $C_2H_5I$ ,  $n-C_3H_7I$ ,  $n-C_4H_9I$ , and  $i-C_4H_9I$ ); and (c) 27 per cent for the secondary iodides ( $i-C_3H_7I$ , and  $s-C_4H_9I$ ). By contrast, all of the primary and secondary chlorides tested ( $CH_3Cl$ ,  $C_2H_5Cl$ ,  $n-C_3H_7Cl$ ,  $i-C_3H_7Cl$ ,  $n-C_4H_9Cl$ ,  $i-C_4H_9Cl$ ,  $s-C_4H_9Cl$ ,  $n-C_5H_{11}Cl$ ,  $i-C_5H_{11}Cl$ ) give organic yields of 21 per cent (31). Tertiary butyl and tertiary amyl chloride, however, each give a yield of about 35 per cent. Apparently the bromides do not exhibit a structural effect similar to the iodides since the organic yields which have been reported are 32, 38, and 33 per cent for  $C_2H_5Br$  (37),  $n-C_3H_7Br$  and  $i-C_3H_7Br$  (36) respectively.

Since the secondary iodides are much less stable than the primary compounds with respect to decomposition to yield hydrogen iodide and the olefin, it is possible that the lower organic yield which they give is attributable to molecules which have just been formed from  $I^{128}$  and have excess energy available. The higher yields of methyl and methylene iodide may result in part, from the fact that they cannot undergo dehydrohalogenation.

It is a remarkable fact that the organic yield of the chlorides is independent of chain length and hence of the ratio of C—Cl bonds to other bonds. As might be predicted from this observation the yield has also been found to be independent of dilution of the chloride in a pure hydrocarbon (31) [see also Miller & Dodson (30)]. It appears that billiard ball collisions between atoms of equal weight do not play any significant part in the process by which the  $Cl^{38}$  from  $Cl^{37}(n, \gamma)Cl^{38}$  enters stable chemical combination.

By contrast with the identity of organic yield shown by the series of dissimilar molecules noted in the last paragraph, attention may be called to the fact that the structurally similar molecules  $C_2H_5Cl$ ,  $C_2H_5Br$ , and  $C_2H_5I$

show markedly differing yields of 21, 32, and 41 per cent respectively (31, 37).

It must be concluded from the observations reported in this section that the chemical characteristics of the medium in which a recoil atom finds itself are of major importance in determining its fate, although physical factors such as its energy, its charge, the strength of cage walls, and the masses of atoms it encounters may also play a role.

*Evidence for a multiplicity of products resulting from (n,  $\gamma$ ) activation.*—By employing carrier separations Gluckauf & Fay (43) showed very early in investigations of reactions activated by the (n,  $\gamma$ ) process in organic halides that bonds could be broken by processes other than a billiard ball collision between two atoms of equal mass. Thus, for example, the  $I^{127}(n, \gamma)I^{128}$  process in liquid  $CH_3I$  was reported to yield 11 per cent of the  $I^{128}$  as  $CH_2I_2$ ; the  $Br^{79}(n, \gamma)Br^{80}$  reaction on  $CH_2Br_2$  produced some  $CHBr_3$ , and that on  $CHBr_3$  produced some  $CBr_4$ . Later, other workers (23, 44) found that when bromine dissolved in  $CCl_4$  is activated by the  $Br^{81}(n, \gamma)Br^{82}$  reaction an appreciable fraction of the  $Br^{82}$  appears as  $CCl_2Br_2$  and another fraction is still higher boiling. This later fraction has been demonstrated to contain  $CBr_4$  and probably also  $CClBr_3$  and  $Br^{82}$ -containing molecules with two carbon atoms. The presence of  $CBr_4$  means that four carbon-chlorine bonds in a single molecule must be broken and replaced by carbon-bromine bonds, one of the latter involving the tagged atom. The presence of this product emphasizes the extremely high energy available to individual molecules, when nuclear processes of activation are used, and the complexity of the elementary processes which may occur.

Further striking evidence of the major rearrangement of bonds that may occur from such activation is furnished by the findings of Fox & Libby (36) that neutron irradiation of propyl bromide yields part of the tagged bromine in each of the following compounds:  $C_2H_5Br$ ,  $i-C_3H_7Br$ ,  $n-C_3H_7Br$ ,  $CH_2Br_2$ ,  $CH_2BrCH_2Br$ ,  $CH_3CHBrCH_2Br$ ,  $CH_2BrCH_2CH_2Br$ , and a fraction with a longer carbon chain.

It has also been shown that  $CCl_2Br_2$  and a more complex product are produced by (n,  $\gamma$ ) activation of  $CCl_3Br$  (38).

*Reactions of halogens activated by the (n,  $\gamma$ ) process in liquid hydrocarbon media.*—The observation of Reid (34)), that iodine activated by the (n,  $\gamma$ ) reaction while in pentane solution can react to enter organic combination (see section on Mechanisms), has been confirmed in two other laboratories (35, 37). Similar results have been found for bromine in pentane (35), for iodine in hexane, heptane, and octane, for halogen originating from ethyl bromide and ethyl iodide in hexane (37, 38), for chlorine from carbon tetrachloride in cyclohexane and in benzene (30), and for chlorine from butyl chloride in heptane (31).

In order to determine whether recoil iodine can rupture carbon-hydrogen bonds, solutions of iodine in liquid methane were irradiated with neutrons

(24). Both  $\text{CH}_3\text{I}$  and  $\text{C}_2\text{H}_5\text{I}$  were formed, indicating that iodine activated by the  $(n, \gamma)$  reaction could cause the rupture of carbon-hydrogen bonds not only in a single molecule but in adjacent molecules. The methane solutions used contained appreciable concentrations of dissolved air. It was also observed that gaseous methane underwent a unique reaction with iodine activated by the  $(n, \gamma)$  process.

The value of the "epithermal reaction" hypothesis in explaining the hydrogen replacement reactions cited above is open to question on the basis of the well-known fact that photochemically and thermally produced bromine and chlorine atoms react with hydrocarbons to form stable hydrogen halide molecules and free radicals, rather than atoms and free radicals (45, 46). There are as yet no experiments which allow a conclusive distinction between the epithermal reaction explanation and the random fragmentation explanation. Possibly as the energetic atom passes through an appropriate energy range it may be able to displace a hydrogen atom from a molecule in an inversion type process. There is the further possibility that internal conversion occurs following recoil so that the final chemical events which lead to stable molecule formation result from charge neutralization processes.

In view of the wide variety of hydrogen replacement reactions now observed to be activated by the  $(n, \gamma)$  process it would be desirable to repeat the often quoted experiment (47) showing that the organic yield of bromine from  $\text{CBr}_4$  dissolved in  $\text{C}_2\text{H}_5\text{OH}$  falls to zero at high dilutions.

*Identification of inorganic products.*—The problem of determining the relative amounts of elemental halogen and hydrogen halide produced in tracer quantities by  $(n, \gamma)$  activated reactions in alkyl halides is complicated by the fact that these species exchange rapidly with each other. Therefore, it is not possible to employ carriers and separate on a macroscopic scale. Attempted separations of gaseous mixtures of hydrogen bromide and bromine by selective reaction of one constituent with freshly reduced copper or with sodium hydroxide pellets have been unsuccessful because both gaseous species reacted with both of these solids (48). Attempts to distinguish the species by the rate at which the inorganic bromine from  $(n, \gamma)$  activation enters organic combination with the medium when heated have likewise proved unsuccessful (48).

A third method (31) makes use of the fact that carefully purified pentene-2 will react instantaneously with tracer amounts of radiochlorine but only very slowly with hydrogen chloride. Using this method it has been found that of the chlorine atoms activated by the  $(n, \gamma)$  process in butyl chloride, about 21 per cent enter organic combination, 8 per cent form  $\text{Cl}_2$ , and 71 per cent form  $\text{HCl}$ .

*Impurity effects.*—Within the last two or three years there has been a growing recognition of the fact that much more than ordinary care must be taken to purify alkyl bromides and alkyl chlorides if correct organic yields are desired in the study of their reactions activated by the  $(n, \gamma)$  process. A number of examples will be quoted here. (a) In 1949 the organic yield of

n-propyl bromide was reported (35) as 50 per cent, using samples which "were redistilled and their refractive indices found to check with those of the pure product within 1 part per ten thousand." In 1952, the same laboratory (36) reported that if the propyl bromide was purified by the more stringent procedure of treatment with ozone followed by distillation and washings, the organic yield was reduced to 35 per cent. (b) The organic yield of ethyl bromide was reported as 75 per cent when not subjected to special purification (37, 47) 65 per cent (49) when "treated with elementary bromine, extracted with sodium sulfite solution, and dried with  $\text{CaCl}_2$ ," and 32 per cent (37) when purified either with ozone or by prolonged mechanical stirring with sulfuric acid. (c) Butyl chloride purified only by brief washing with sulfuric acid and distillation regularly gave organic yields of about 30 per cent. When prepared by ozone treatment or vigorous mechanical stirring with 95 per cent sulfuric acid for several days, the yield was reproducibly 21 per cent (31). Purified samples which gave this result immediately after purification again gave high results after several days standing in air in a glass stoppered bottle in the dark. The regeneration of impurity was presumably due to a slight dehydrohalogenation or hydrolysis of the chloride. (d) Samples of propyl bromide, which were carefully distilled, were observed to show progressively higher organic yields with increasing time of standing after irradiation (35), whereas this was not the case if purification by ozone treatment was used (36). Similarly, the inorganic activity from the ( $n$ ,  $\gamma$ ) reaction on ethyl bromide (49, 50), ethyl iodide (50, 51), and iodobenzene (52) has been reported to "exchange" back into organic combination at a measurable rate but no such effect was observed with samples of ethyl bromide and ethyl iodide which had undergone more rigorous purification (22, 37).

The concentrations of impurity which may be serious in work of this type are so low as to be undetectable by ordinary criteria such as melting point, refractive index, and light absorption measurements. In general the identity of the impurities is not known and there is no possibility of designing a purification procedure with complete certainty that it will give a pure product, or even that it will not introduce more impurity than it removes. There are, however, several criteria which may be applied as indicative of the fact that impurities have been reduced to a level where they do not influence the results. These include the following: (a) Identical results are obtained with reagents purified by widely different methods; (b) Several different but related compounds (which would presumably contain different amounts and types of impurity before purification) give identical results (22); (c) the organic products are characterized and found to be such that they could not have been formed by reaction with any conceivable impurity.

#### REACTIONS IN SOLID ORGANIC MEDIA

Because nuclear transformations are unaffected by temperature and because the energy of recoil or charge which they may give to atoms is so much in excess of chemical bond energies, it might be expected that the chemical



reactions which they initiate would likewise be temperature independent. In early work this was shown to be true, at least qualitatively, for the isomeric transition activated reaction of bromine with carbon tetrachloride (53) in the range from room temperature to  $-190^{\circ}$ . The organic yield was, however, lower for reactions carried out just below the freezing point than for those carried out just above. This fact indicated a phase effect which might have been attributable to the density or crystal structure of the solid as compared to the liquid, or to partial fractional crystallization of the bromine into clumps of molecules during freezing of its carbon tetrachloride solution.

Conclusive and extensive evidence for the existence of a phase effect, in the  $(n, \gamma)$  activated reactions of the bromine in the propyl bromides, was provided by the work of Friedman & Libby (35), and Fox & Libby (36). They showed that the organic yield of *n*-propyl bromide increases from about 39 to 88 per cent when the irradiation is carried out in the solid phase rather than the liquid phase at the freezing point ( $-110^{\circ}$ ) and that a similar effect occurs with *i*-propyl bromide. Fractionation experiments with added carriers showed that the yields of the eight different organic products identified were affected differently by the phase change, the increase varying from a factor of 1.7 to 9.4. In the absence of a phase change there was little or no change in yield with change in temperature for either compound. The results were of major interest because it seemed that they might provide clues both as to the effects of the phase on chemical reactions in general and as to the nature of the elementary processes by which recoil atoms or charged atoms become chemically stabilized.

It was of immediate importance to know whether the phase effects were general for many compounds, whether they occurred for elements other than bromine, and whether they occurred for methods of activation other than the  $(n, \gamma)$  process. The initial answer to all of these questions was affirmative. It was shown that the organic yields of the  $(n, \gamma)$  reaction on the bromine in  $\text{CCl}_3\text{Br}$  and  $\text{CCl}_2\text{Br}_2$  (38), on the bromine in  $\text{CF}_3\text{Br}$  (32), on the chlorine in  $\text{CCl}_4$  and  $\text{CCl}_2\text{Br}_2$  (38), on the chlorine in  $\text{C}_2\text{H}_5\text{Cl}$ , *n*- $\text{C}_3\text{H}_7\text{Cl}$ , *n*- $\text{C}_4\text{H}_9\text{Cl}$ , *s*- $\text{C}_4\text{H}_9\text{Cl}$ , *i*- $\text{C}_4\text{H}_9\text{Cl}$ , *i*- $\text{C}_6\text{H}_{11}\text{Cl}$  and *s*- $\text{C}_6\text{H}_{11}\text{Cl}$  (31), and on the iodine in  $\text{CH}_3\text{I}$ ,  $\text{CH}_2\text{I}_2$ , *n*- $\text{C}_3\text{H}_7\text{I}$ , *i*- $\text{C}_3\text{H}_7\text{I}$ , and *n*- $\text{C}_4\text{H}_9\text{I}$  (22) were all higher in the solid phase than the liquid, although the magnitude of the change varied from compound to compound. The organic yield from the isomeric transition (38) of bromine in the  $\text{CCl}_3\text{Br}$  molecule was found to be higher in the solid than the liquid.

However, there were also, results in contrast to those found with the propyl bromides. For example, the compounds  $\text{C}_2\text{H}_5\text{I}$ , *i*- $\text{C}_4\text{H}_9\text{I}$ , and *s*- $\text{C}_4\text{H}_9\text{I}$  showed little or no change in organic yield with change in phase (22). A second different type of behavior was evidenced in experiments in which the organic yield of bromine activated by either neutron capture or isomeric transition in  $\text{CCl}_3\text{Br}$  increased with decreasing temperature below the freezing point (38). Another contrasting finding was the observation that the



ratio to each other of the organic products from the  $(n, \gamma)$  reaction on the bromine of  $\text{CCl}_3\text{Br}$  was essentially the same in the solid as in the liquid, although the total yield was higher in the solid.

Very recently Rowland & Libby (54) have reported that the organic yield of the  $\text{Br}^{81}(n, \gamma)\text{Br}^{82}$  reaction in  $n\text{-C}_4\text{H}_9\text{Br}$  at  $-196^\circ$  is 66 per cent if the solid is in the glassy form whereas it is 92 per cent if it is in the crystalline form. They have also found that the organic yields of  $\text{Br}^{82}$  are different from those of  $\text{Br}^{80m}$  in six crystalline bromides tested but that there is no difference between the two isotopes in four glassy bromides tested.

Libby & co-workers (35, 36, 54) have developed a hypothesis which, with the postulates made, will explain the results they have observed. It pictures the energetic recoil atom as giving up its energy in successive collisions with atoms of the solid. These atoms in turn, transfer energy to other atoms or molecules in such a manner as to melt a pear shaped region of the solid with a volume of about 1000 molecules. In some cases the tagged atom will transfer nearly all its energy to another bromine atom while it still has high energy. In this case it will be stopped and will enter chemical combination in the middle of the molten region. The authors suggest that such events should not be greatly different in a frozen medium than in a liquid medium. If, however, the recoil atom loses its energy a little at a time, it may rupture a molecule in an epithermal collision and combine with one of the radicals formed. Such events occur near the periphery of the molten region where the cage wall is apt to be much stronger in a frozen medium than in a liquid medium. Hence the authors suggest that the solid phase will favor organic combination. The authors have presented a somewhat detailed analysis of the phase effect on different products of the  $(n, \gamma)$  reaction on propyl bromides in terms of this model of the reaction processes.

Among the questionable postulates of this theory (see "Proposed Mechanisms" is the assumption that a strengthened cage wall will favor organic combination rather than inorganic combination of the tagged atom, since it has been shown that both inorganic and organic combination occur in both the high-energy and thermal regions (37). Among the unexplained facts are the failure of some compounds to show an increase in organic yield in the solid state (22), and the lack of correlation between yield and density (22) in some cases.

According to the "nest of radicals" or "random fragmentation" hypothesis, both the higher organic yields observed for some compounds in the solid state relative to the liquid and the accompanying changes in the relative percentages of different products are explicable on the following bases: (a) The relative probability of different types of bond rupture being produced by the energetic atom varies with the density and crystal structure of the medium; (b) there are differences in the relative probability of organic and inorganic fragments diffusing away from the immediate vicinity of the cooled tagged atom. The net influence of such effects on the organic yield would be expected to vary from compound to compound. The difference in

orientation of the molecules relative to each other in the crystalline and glassy states might also be expected to alter the relative amounts of different stable products formed.

#### GAS PHASE REACTIONS

*Efficiency of rupture of parent bond following ( $n, \gamma$ ) process.*—The total energy of the  $\gamma$ -rays emitted in the radiative neutron capture process with slow neutrons is 5 to 10 Mev. (55). The recoil energy received by the product nucleus as a result of equating momentum with a photon of this energy is of the order of 100 ev. In all molecules except those where the recoiling nuclide is heavy and is combined only with a single hydrogen atom (56) this should always cause the radiating atom to split its chemical bonds, unless the  $\gamma$ -ray energy is emitted in a cascade with large cancellation of momentum.

That the ( $n, \gamma$ ) events on  $\text{Br}^{79}$  are in fact nearly 100 per cent efficient in causing bond rupture is shown by the observation of Wexler & Davies (19) that less than 1 per cent of the  $\text{Br}^{80m}$  (4.4 hr.) produced by neutron irradiation of ethyl bromide gas at  $3\mu$  pressure was retained in organic combination. Libby (28) had previously found a value of 5 per cent for the same reaction at higher ethyl bromide pressures and Suess had reported 3 per cent from measurements made on the  $\text{Br}^{80}$  (18 min.) isomer (27). It has been shown that less than 2 per cent of the  $\text{Cl}^{38}$  activity from neutron irradiation of gaseous butyl chloride (31) and less than 1 per cent of the  $\text{Br}^{82}$  from the irradiation of low pressures of  $\text{CF}_3\text{Br}$  (32) fail to rupture the parent bond.

Williams & Hamill (29, 41) have found that some 25 per cent of the  $\text{Br}^{80}$  atoms resulting from the  $\text{Br}^{79}$  ( $n, \gamma$ )  $\text{Br}^{80}$  (18 min.) process in a system containing 170 mm. of hydrogen bromide and a few mm. of  $\alpha, \beta$ -dibromoethylene remain in inorganic combination. Having established that all thermalized bromine atoms would enter organic combination by exchange with the olefin in this mixture, they interpret their result to indicate that either an appreciable fraction of the hydrogen bromide bonds are not ruptured by the ( $n, \gamma$ ) process, or that recoil bromine atoms undergo "hot" exchange reactions with hydrogen bromide before they become thermalized.

*Evidence for "hot" atom reactions.*—There is continually growing evidence from studies in photochemistry (57, 58, 59, 60) and radiation chemistry (61, 62) that "hot atom" and "hot radical" reactions may be important in these fields. The enhanced reactivity of hot atoms and radicals may be attributable to electronic excitation, charge, or kinetic energy. As a result of its special activation, the hot radical is capable of attacking a molecule in such a way as to incorporate itself in a stable product, usually leaving another radical as the second product. This can take place in an encounter between an isolated gas phase molecule and the hot atom or radical as well as in the liquid phase.

There is evidence for hot reactions of this sort on the part of atoms activated by nuclear transformations. In the liquid phase it is impossible to distinguish them from reactions of the atoms with radicals which they have formed. In the gas, however, where the latter type of reaction does not

occur, the "hot" reactions can be identified. Williams & Hamill (29) have reported rather convincing evidence that about 13 per cent of the bromine atoms activated by the  $\text{Br}^{79}(n, \gamma)\text{Br}^{80}$  (18 min.) process in ethyl bromide at 200 mm. pressure form hydrogen bromide by a hot reaction ( $\text{Br} + \text{RH} \rightarrow \text{R} + \text{HBr}$ ) before they have been thermalized. Tests by Hamill & Young (41) on the reaction of bromine atoms produced from gaseous  $\text{CH}_3\text{Br}^{80m}$  by isomeric transition have been interpreted to indicate that some of the atoms form hydrogen bromide or exchange with it by a hot reaction.

There is evidence that 1 to 3 per cent of the recoil halogen atoms from neutron irradiation of gaseous ethyl bromide (29) and gaseous ethyl iodide (24) at about 100 mm. pressure may re-enter organic combination by hot processes.

Iodine atoms activated by the  $\text{I}^{127}(n, \gamma)\text{I}^{128}$  process have been found to undergo an unexpected, high yield, hot atom reaction with methane (24). About 45 per cent of the neutron capture events produce  $\text{CH}_3\text{I}^{128}$ . The reaction must occur in an inversion type step between a hot  $\text{I}^{128}$  and a methane molecule rather than by a free radical mechanism because the presence of a large excess of photochemically produced iodine atoms tagged with  $\text{I}^{131}$  in the system does not alter the reaction of the  $\text{I}^{128}$  nor does any of the  $\text{I}^{131}$  enter organic combination. The authors suggest that the reaction occurs as an indirect result of the charge acquired by 50 per cent of the  $\text{I}^{128}$  atoms as a result of internal conversion of part of the energy of the  $(n, \gamma)$  process rather than wholly as a result of the kinetic energy. Preliminary experiments on the effect of added inert gases, and of molecules with lower ionization potential than iodine atoms, tend to support this conclusion (63a). It is further supported by the fact that bromine activated by isomeric transition will react with methane to form methyl bromide (63b). It is interesting to note that the  $(n, \gamma)$  activated reaction of  $\text{I}^{128}$  with methane is specific, i.e., very little reaction occurs with ethane or methyl iodide (63a).

*Organic yield as a function of gas density at high pressures.*—A few experiments have been made (32) to study the effect of change in density on organic yield at constant temperature in a gas at high pressures near its critical point. Sealed quartz tubes containing  $\text{CF}_3\text{Br}$  plus 1 mole per cent  $\text{Br}_2$  at densities of 0.47, 0.58, 1.001, and 1.16 gm./cc. and irradiated with neutrons at 70°C. gave organic yields of 4.2, 5.3, 7.0, and 9.9 per cent respectively, thus seeming to indicate an increase in yield proportional to the increase in density. A possible explanation of this effect is that the diffusion coefficients of the organic radicals which the energetic atom forms around itself are decreased more by an increase in density than are the diffusion coefficients of the inorganic fragments.

It should be noted in this connection that a knowledge of the density change which accompanies a phase change does not in general make it possible to predict even qualitatively the change in organic yield caused by the phase change (22).

*Reactions of thermalized atoms produced by the  $(n, \gamma)$  and isomeric transition*

*process in the gas phase.*—Neutron irradiation of a halogen compound present at low mole fraction in an inert gas with a lower ionization potential than the halogen should, in principle, allow the generation of tracer concentrations of neutral thermal halogen atoms in thermal equilibrium with the gas. Such a system would in many respects be ideal for studying the relative rates and activation energies of different halogen atoms with different compounds.

This approach to the study of thermal atom reactions has not yet been exploited systematically. Williams & Hamill (29) and Hamill & Young (41) have, however, studied the combination of hot and thermal reactions which occur following the ( $n, \gamma$ ) and isomeric transition reactions of bromine in various mixtures of gaseous ethyl bromide, hydrogen bromide, ethylene, methyl bromide, and bromoolefins and have been successful in rationalizing the results in terms of a kinetic treatment which distinguishes the hot from the thermal processes.

#### REACTIONS INITIATED BY ISOMERIC TRANSITION

Relatively few studies of reactions activated by isomeric transition have been made compared to the number of investigations using ( $n, \gamma$ ) activation. In the last few years, these studies have dealt mainly with the isomeric transition of  $\text{Br}^{80m}$ . Some, such as the demonstration of a phase effect (38) and the study of reaction kinetics in gaseous mixtures of hydrogen bromide and olefins (41), have been referred to above. In a different type of investigation Coffin & Jamieson (64) have determined the fraction of  $\text{Br}^{80m} \rightarrow \text{Br}^{80}$  events which yield bromine bound in the tetrahalide molecule for solutions of bromine in carbon tetrachloride, silicon tetrachloride, germanium tetrachloride, and tin tetrachloride. No correlation of the yields with the bond strengths, ionic character, or densities of the four compounds was found. Other recent studies of reactions activated by isomeric transition will be discussed under the headings below.

*Mechanism of chemical activation by the isomeric transition of  $\text{Br}^{80m}$ .*—When  $\text{Br}^{80m}$  (4.4 hr.) undergoes isomeric transition to its ground state,  $\text{Br}^{80}$  (18 min.), it essentially always becomes positively charged as the result of the loss of either one or two conversion electrons and of Auger electrons. The average charge is plus 10 (25). The conversion electrons and Auger electrons do not impart sufficient recoil energy to the atom to be chemically significant (65), but the positive bromine ion usually splits out of its parent compound and may thereafter react with other molecules of the medium to form new compounds. An initial attack on the theory of this type of bond rupture and subsequent reaction has been made by Magee & Gurnee (66). They point out effects which may lead to chemical reaction. (a) The positive charge produced by the transition may lead to a polar state of the molecule with resulting dissociation attributable to coulombic forces. They find, however, that the lowest electronic states of simple  $\text{HBr}^{+x}$  molecules may be homopolar states which are stable with respect to dissociation into  $\text{H}^+$  and  $\text{Br}^{+(x-1)}$ . (b) The charged molecule-ion may be partially neutralized in a

collision with a neutral molecule and gain both excitation energy and kinetic energy from the encounter. This kinetic energy may easily be of the order of tens of electron volts. (c) Atom or molecule ions with energy from the charge transfer process may react with neutral molecules.

*Partial failure of bond rupture following isomeric transition.*—The efficiency of the  $\text{Br}^{80}$  isomeric transition in splitting the atom from its parent molecule has now been determined for several compounds. The values, listed as per cent failure to rupture, are as follows: gaseous  $\text{HBr}$ , 25; gaseous  $\text{DBr}$ , 16 [Hamill & Young (41)]; gaseous  $\text{CF}_3\text{Br}$ , 1; gaseous  $\text{CH}_3\text{Br}$ , 6;  $\text{CH}_3\text{Br}$  in liq.  $\text{Br}_2$ , 6; gaseous  $\text{CCl}_3\text{Br}$ , 7;  $\text{CCl}_3\text{Br}$  in liquid  $\text{Br}_2$ , 13;  $\text{C}_6\text{H}_5\text{Br}$  in liquid  $\text{Br}_2$ , 13 (67); aqueous  $\text{Co}(\text{NH}_3)_5\text{Br}^{+2}$ , 0; solid  $\text{Co}(\text{NH}_3)_5\text{Br}(\text{NO}_3)_2$ , 14; aqueous  $\text{PtBr}_6^{-2}$ , 53; solid  $(\text{NH}_4)_2\text{PtBr}_6$ , 100 [Adamson & Grunland (68)]. In all of these experiments the conditions were designed to prevent re-entry into the parent compound. The results indicate that the stability of the parent molecule or ion to dissociation after one of its atoms has undergone isomeric transition may be dependent both on its composition and on whether it is in the gaseous state or is in close proximity to other molecules in the liquid state.

*Collection of charged daughters of  $\text{Br}^{80m}$  isomeric transition.*—Despite the fact that it is now well established by both physical and chemical tests that nearly every  $\text{Br}^{80m}$  which undergoes isomeric transition emits a conversion electron, with the result that the daughter must have a positive charge, only one successful direct demonstration of the charge has been achieved. Wexler & Davies (69) placed ethyl bromide at a few microns pressure, containing  $\text{C}_2\text{H}_5\text{Br}^{80m}$  at high specific activity, between concentric cylindrical electrodes under conditions such that mean free path as estimated for Van Der Waals collisions was of the order of the distance between the electrodes. Under these conditions about 50 per cent of the  $\text{Br}^{80}$  daughter atoms could be collected preferentially on the negative electrode.

Attempts have been made (32b) to find a solid brominated surface from which the isomeric transition daughters can escape into a vacuum surrounding the sample and to detect the positive charge, if any, on these escaping daughters. Surfaces of ceresin wax and of methyl siloxane which had been photobrominated with  $\text{BrBr}^{80m}$  were found to emit  $\text{Br}^{80}$  (18 min.) daughter activity which could be collected on metal foils in an evacuated system. The amount of such activity was, however, much in excess of that which was produced in the upper monolayer of the surface and less than a quarter (possibly none) of it was charged. Similar results were obtained with the bromine in the form of 2,4,6-tribromo-3-hydroxyquinolate. When the bromine was in the form of sodium bromide or silver bromide no transition daughter atoms were emitted from the surface. Using the transition daughter atoms emitted from the organic surfaces it was possible to determine the sticking coefficients for such atoms colliding with specified surfaces (32b, 70).

*Comparison of results of activation by radiative neutron capture and by isomeric transition.*—If, as has usually been assumed the chemical effects



resulting from ( $n, \gamma$ ) activation are attributable to the recoil energy of the atom and those resulting from activation by isomeric transition to the charge on the atom, it is plausible to suppose that the products obtained would be different in the two cases. If, however, atoms which have undergone isomeric transition react to enter stable combination as a result of recoil energy which they gain from charge transfer processes (66, 69), or atoms which have been activated by the ( $n, \gamma$ ) process finally react because of the charge gained from internal conversion (19, 20), then the products might be similar. Careful comparison of the two methods of activation has been made in only a few systems. The data are, however, adequate to indicate that the two modes of activation do not give identical results in all cases, although they are essentially indistinguishable in others.

The system which has shown the most highly selective differences is that of bromine reacting with toluene. Gavoret & Ivanoff (71) have reported that the toluene bromide/benzyl bromide ratio is 0.12 when activation is by the isomeric transition and 0.8 when it is by neutron capture. In each case the ortho/para/meta ratio in the toluene bromide was 4 to 2 to 1.

Another case of a pronounced difference in yield has been observed in mixtures of bromine and tetrachloroethylene. These mixtures gave organic yields of 37 per cent in solution and 0 per cent in the gas phase when the bromine was activated by the ( $n, \gamma$ ) process, in contrast to 85 per cent in solution and 19 per cent in the gas phase when activation was attributable to isomeric transition (44, 72). The isomeric transition activation of the bromine in bromotrichloromethane gave higher organic yields in both the liquid and the solid phases than did ( $n, \gamma$ ) activation (38). The same effect, though less marked, was observed for the reaction of bromine with liquid carbon tetrachloride (23, 44).

The most remarkable similarity in the effects of the two modes of activation has been observed in a careful analysis of the relative amounts of  $\text{CCl}_3\text{Br}$ ,  $\text{CCl}_2\text{Br}_2$ , and higher boiling products produced by each method, as a function of  $\text{Br}_2$  concentration in  $\text{CCl}_4$ . Within experimental error the ratios of different organic products resulting from the two methods of activation are identical at all concentrations. This must mean either that the physical processes which lead to organic combination in carbon tetrachloride, following the two modes of activation, are the same or that the molecule is so simple that it is ruptured in the same way by two different types of process (i.e., involving recoil energy in one case and charge neutralization in the other).

#### REACTIONS INVOLVING OXY-ANIONS OF INORGANIC SALTS ACTIVATED BY THE ( $n, \gamma$ ) PROCESS

When crystalline salts containing oxy-anions are irradiated with neutrons and subsequently dissolved in aqueous solution it is usually found that some of the atoms which have undergone the ( $n, \gamma$ ) process remain in the form of the parent anion while others are reduced. Investigators in the field have sought to deduce information about the bond rupture processes by studying



the effects of different variables on the percentage yield of the parent species (often called the "retention"). These variables include exposure to elevated temperature and to  $\gamma$ -radiation during and after radiation, and variations in the oxidation-reduction potential, pH and carrier content of the solvent. In addition, studies have been made of the irradiation of dissolved salts under a variety of solvent conditions.

*Effect of temperature and  $\gamma$ -radiation on yields of parent species in solids.*—Heating of neutron irradiated crystals prior to dissolving has been observed to increase the yield of the parent form of the anion in the case of  $K_2CrO_4$  by Green & Maddock (73); in the case of  $KMnO_4$  by Rieder, Broda & Erber (74) and Aten & van Berkum (75); in the case of  $KBrO_3$  by Cobble & Boyd (16); and in the case of  $NaIO_3$  and  $NH_4IO_3$  by Cleary, Hamill & Williams (76). The latter two groups of authors have also shown that the retention by the bromate and iodates is increased by  $\gamma$ -irradiation following neutron irradiation. Cobble & Boyd (16) have determined the rates of thermal and radiation induced decomposition of potassium bromate. They have found that the return of recoiled radiobromine atoms to bromate, under the influence of heat or  $\gamma$ -radiation, occurs at the same time the bromide content of the crystals is increasing because of decomposition induced by either temperature or radiation. The effects were observed at 80° and above, and at gamma intensities of the order of 16,000 r/min. The results argued strongly that some of the recoil bromine atoms resided in the crystal in a metastable situation different from the bromine species liberated by radiation-decomposition. This species was shown to persist in the crystal for long periods of time at room temperature (77).

In order to determine whether all of the parent yield from  $KBrO_3$  was attributable to recombination caused by the  $\gamma$ -radiation of the pile, samples were irradiated for 1, 5, 10, and 20 sec. The retention extrapolated to zero time was about 9 per cent. The cause of this "non-rupturing" fraction is not certain. It may be attributable to one or more of the following: cancellation of momenta from a multiplicity of  $\gamma$ -rays in a single cascade; internal conversion of part of the neutron capture energy, thus leaving a highly charged bromine ion which finally stabilized as bromate; a certain probability that the recoil atom ruptured the surrounding lattice in such a way that the fragments reformed stable bromate.

*Effect of medium on parent yield in aqueous solution.*—Muller & Broda (78a) report that the distribution of activity between As (III) and As (V) following irradiation of solutions, of either arsenite or arsenate, is independent of temperature, pH, and concentration. This suggests that the valence of the radioion produced is determined during the explosion of the ion following neutron capture rather than by subsequent chemical effects. By contrast other ions such as  $MnO_4^-$  (47, 74, 75) and  $IO_3^-$  (76) give yields which depend on the nature of the medium in which the salt is irradiated. For example, Cleary, Hamill & Williams (76) find 20 per cent retention as  $IO_3^-$  from neutron irradiated solutions of  $NaIO_3$  over a wide range of con-

centration and pH. However, this yield can be reduced to 6 per cent by addition of  $I^-$  or  $CH_3OH$  and it can be raised to 40 per cent by the presence of  $IO_4^-$ . These authors give a kinetic interpretation of their data in terms of competing reactions involving a fraction of the recoil atoms which form an unstable intermediate.

*Other results.*—Included in other recent work on the  $(n, \gamma)$  activated reactions of oxy-anions are: the study of the distribution of  $P^{32}$  activity between orthophosphate, pyrophosphate, phosphite, and hypophosphite following neutron irradiation of  $Na_4P_2O_7 \cdot 10H_2O$ ,  $Na_4B_2O_7$ , and  $Na_2HPO_4 \cdot H_2O$  by Aten, van der Straaten & Rieseboos (78b); an investigation of the chemical species containing  $P^{32}$  in neutron bombarded calcium phosphates by Fiskell, DeLong & Oliver (79, 80); a determination of the Szilard-Chalmers reaction yields of Cr(III) from solid  $K_2Cr_2O_7$  and  $K_2CrO_4$  by Kahn, Freedman & Bryant (81); and investigation of the yields of irradiated permanganate solutions as a function of concentration and neutron energy by Rieder (82).

#### REACTIONS INVOLVING A CHANGE IN ATOMIC NUMBER OF THE REACTING ATOM

In contrast to  $(n, \gamma)$  activation, the activation processes with which this section is concerned all involve particle emission from the nucleus and hence the recoil energies are in general much higher. There appears to be no reason why the ultimate chemical products should be different than if an atom of the same final atomic number were activated by the  $(n, \gamma)$  process.

*Properties of sulfur atoms produced by the  $CP^{35}(n, p)S^{35}$  reaction in alkali chlorides.*—Several laboratories [(83), Koski (84) Croatto & Maddock (85), and Wilk (86)] have observed that when KCl crystals are exposed to neutrons, without exclusion of air, and then dissolved in water (containing  $S^{2-}$ ,  $SO_3^{2-}$ , and  $SO_4^{2-}$  as carriers), the  $S^{35}$  appears as  $SO_4^{2-}$ . Koski (84) has shown that if stringent methods are used to degas the crystals, prior to irradiation, 35 per cent of the  $S^{35}$  can be recovered in sulfide carrier. However, Croatto & Maddock (85) have been unable to obtain any product other than sulfate even though apparently rigorous degassing precautions were taken. More recent work (87) using vacuum sublimed crystals and thoroughly degassed carrier solutions has succeeded in recovering 90 per cent of the activity as sulfide when the crystals are dissolved in aqueous sulfide. When the carrier is added after dissolving the crystals in water, about 30 per cent of the activity appears as sulfide and the remainder is oxidized to sulfate. The difference of 60 per cent is ascribed to a highly reactive form, possibly  $S_1^0$ , which is readily oxidized by water. Contrary to other reports (85), the later work (87) shows no difference in behavior between potassium chloride and rubidium chloride.

*Products formed by  $C^{14}$  from the  $N^{14}(n, p)C^{15}$  reaction.*—Yankwich, Rollefson & Norris (88), and Yankwich (89, 90) have found that the products formed by  $C^{14}$  from the  $N^{14}(n, p)C^{14}$  reaction on  $NH_4NO_3(NH_2)_2CO$ ,  $N_2H_4$

.2HCl,  $\text{NH}_2\text{CH}_2\text{COOH}$ ,  $\text{C}_5\text{H}_5\text{N}$ ,  $\text{C}_6\text{H}_5\text{NH}_2$  (88),  $\text{Be}_3\text{N}_2$  (89),  $\text{NH}_4\text{Cl}$ ,  $\text{NH}_4\text{Br}$  (90) may include  $\text{CO}_2$ ,  $\text{CO}$ ,  $\text{CH}_4$ ,  $\text{HCN}$ ,  $\text{CH}_3\text{OH}$ ,  $\text{HCOOH}$ , and  $\text{CH}_3\text{NH}_2$  and depend on the target substance and sometimes on reaction occurring on dissolution in water following irradiation. Norris & Snell (91) have found 56 per cent  $\text{CO}$  and 44 per cent  $\text{CO}_2$  with less than 2 per cent of other  $\text{C}^{14}$  products from neutron irradiated  $\text{NH}_4\text{NO}_3$  solutions. Croatto, Giacomello & Maddock (92) report that the  $\text{C}^{14}$  produced by neutron irradiation of quino-line oxalate is distributed as follows: 8.4 per cent in naphthalene; 2.2 per cent in  $\alpha$ -naphthol; 7.1 per cent in oxalic acid; 1.6 per cent in quinoline, and the remainder in a basic mixture. Edwards (93), who has conducted an investigation of the efficiency of exchange of atoms produced by the ( $n$ ,  $p$ ) process with bound atoms as a function of bond type and medium, finds that not more than 0.5 per cent of recoil  $\text{C}^{14}$  atoms exchange with normal carbon atoms of the pyridine ring.

*Activation by  $\beta$ -decay.*—Atoms which undergo negatron or positron emission receive recoil energy which varies from zero to a maximum value because of neutrino emission. Electronic excitation or ionization may possibly occur also. If this does not happen the daughter of negatron emission will be born with an oxidation number one higher than the parent and the daughter of positron emission with an oxidation number one lower. The oxidation number achieved after interaction with the medium will depend on the activation given by the nuclear process, and on the chemical characteristics of the medium and of the species formed. Only those beta emitters which form a radioactive daughter are convenient for study.

Two papers dealt with this subject prior to 1950 (94, 95). More recently Burgus & Kennedy (96) have investigated the chemical state of  $\text{Cr}^{51}$  formed by the decay of  $\text{Mn}^{51}$  in manganous and permanganate solutions. With carriers present for Cr (III) and Cr (VI) the manganous solutions yielded almost exclusively Cr (III) while the permanganate solutions yielded about equal amounts of each of the two oxidation states. Keneshea & Kahn (97) have studied the chemical forms of  $\text{I}^{131}$  produced by the  $\beta$ -decay of  $\text{Te}^{131}$ , which was in turn produced by irradiating organic solutions of  $\text{TeCl}_4$  with neutrons. Organic yields of  $\text{I}^{131}$  observed were 40, 30 and 13 per cent in  $\text{C}_6\text{H}_5\text{Cl}$ ,  $\text{C}_6\text{H}_5\text{I}$ , and  $\text{C}_6\text{H}_6$  respectively. Of the 13 per cent, 10 seemed to be iodobenzene and the remainder higher boiling compounds. Edwards (98) has investigated the bond rupture caused by the decay of  $\text{Pb}^{210}$  in lead tetramethyl to  $\text{Bi}^{210}$ , in both liquid and gaseous systems.

*Activation by other processes involving change in atomic number.*—Meier & Garner (99) have found that the  $\text{Cl}^{34}$  activity produced by the  $\text{S}^{34}(p, n)\text{Cl}^{34}$  reaction in  $\text{Na}_2\text{SO}_4$  and  $\text{K}_2\text{S}_2\text{O}_8$  crystals is essentially all in a form indistinguishable from  $\text{Cl}^-$  rather than  $\text{ClO}_3^-$  or  $\text{ClO}_4^-$ .  $\text{P}^{32}$  produced by the  $\text{Cl}^{35}(n, \alpha)\text{P}^{32}$  reaction on alkali chlorides is divided about evenly between P(V) and lower valences. The ratio of P(V) to lower valences is increased by the presence of water in the crystals but decreased by heating at  $350^\circ$ , which removes the color induced by irradiation [Caillat & Sue (100, 101)].

REACTIONS INDUCED BY THE ( $\gamma$ ,  $n$ ) PROCESS

Very few investigations of this mode of activation have been made. They include a test of the retention of copper in the organic fraction following the  $\text{Cu}^{63}(\gamma, n)\text{Cu}^{62}$  reaction on copper salicylaldehyde-*o*-phenylenediimine, by Holmes & McCallum (102), who obtained results similar to those obtained earlier by Duffield & Calvin (103) by the ( $n$ ,  $\gamma$ ) reaction on the same compound. Experiments were made both with the solid compound and with pyridine solutions. More recently Rowland & Libby (104) have made interesting observations on the effect of phase on the  $\text{C}^{11}$  products formed as a result of the  $\text{C}^{12}(\gamma, n)\text{C}^{11}$  reaction. Using radiation such that the recoil energy of the  $\text{C}^{11}$  was calculated to be in excess of  $10^5$  ev, they have found that solid  $\text{CO}_2$  at  $-78^\circ$  yields about equal amounts of  $\text{C}^{11}\text{O}_2$  and  $\text{C}^{11}\text{O}$  whereas liquid  $\text{CO}_2$  at  $25^\circ$  yields at least 95 per cent CO. Powdered  $\text{NaHCO}_3$  yields about equal amounts of the two oxides but  $\text{NaHCO}_3$  or  $\text{Na}_2\text{CO}_3$  in water yields only CO. It appears that in the solid phase the thermalized C atoms are confined in sufficiently close proximity with radicals which they have formed to have a significant chance of recombining with them to form  $\text{CO}_2$ .

EVIDENCE OF FAILURE OF BOND RUPTURE FOLLOWING THE ( $n$ ,  $\gamma$ ) PROCESS IN COMPLEX MOLECULES

Anderson & Delabarre (105) have reported the remarkable result that 80 per cent of the  $\text{Co}^{60}$  formed by the  $\text{Co}^{59}(n, \gamma)\text{Co}^{60}$  reaction on crystalline vitamin  $\text{B}_{12}$  remains in the parent molecule. Careful separation procedures were used and the biological effectiveness of the product was tested. This phenomenon is worthy of further investigation using dissolved as well as crystalline compounds. A similar surprisingly high retention has been reported by Ball, Solomon & Cooper (106) for  $\text{S}^{35}$  formed by the  $\text{S}^{34}(n, \gamma)\text{S}^{35}$  reaction in cystine. A subsequent investigation of the latter reaction by Lipp & Weigel (107) failed to confirm the earlier results however. In this work, the irradiated cystine was highly purified by several precipitations and successive transformations to benzylcysteine, cysteine, and cystine. As would be expected from the high recoil energy of the  $\text{S}^{35}$  none was found in the purified product.

There are several reports in the literature of the activity recovered in the inorganic fraction following neutron irradiation of complex molecules. The emphasis in these cases is placed on the yield and enrichment of inorganic activity resulting from the Szilard Chalmers process; the organic fractions were not purified to determine the retention in the parent form. For example, Herr (108) found the inorganic yields of the radioactive metals from neutron irradiation of V, Mo, Pd, Os, Ir, and Pt phthalocyanines to be about 90 per cent for the light and medium weight elements but only about 12 per cent for the platinum and iridium phthalocyanines. Spano & Kahn (109) found that 50 per cent of the radiotin produced in the neutron irradiation of tetraphenyl tin could be extracted as inorganic tin. Melander (110) has used uranyl

salicylaldehyde-o-phenylenediimine for preparation of high specific activity  $U^{239}$  and  $Np^{239}$  by the Szilard Chalmers process in a manner similar to that used earlier for the copper compound (102, 103), and referred to in a previous section.

#### NEUTRON ENERGY EFFECTS AND ISOTOPE EFFECTS

Very few investigations reported in the literature have been devoted to searching for neutron energy effects or isotope effects on  $(n, \gamma)$  activated reactions. Many observations incidental to other investigations have indicated that such effects are not common. For example, in the author's laboratory it has been observed that various pure alkyl halides give the same organic yield when irradiated with a Ra-Be source or Sb-Be photoneutron source (with or without moderator), or in the thermal column of a nuclear reactor, or in other positions in the nuclear reactor. This result seems eminently reasonable since the chemical fate of the recoil atom must be determined after it has lost most of its energy and therefore might not be expected to be influenced by changes in the relatively large initial energy. It has also been observed that  $Br^{80m}$  and  $Br^{82}$  give the same organic yields in many reactions.

There are, however, a few investigations reported which deal specifically with these matters and in some cases suggest conclusions which conflict with those cited above. Capron & Crevecoeur (111) report that when  $C_6H_5Br$  is irradiated with neutrons from a Ra-Be source at a distance of 2 cm. through paraffin the organic yield of  $Br^{80}$  (18 min.) is 50 per cent and that of  $Br^{80m}$  (4.4 hr.) is 65 per cent. The ratio of the retentions,  $r$  (18 min.)/ $r$  (4.4 hr.), varies with distance through paraffin from the source, either with or without cadmium intervening. This effect is attributed by the authors to variations in the recoil energy of the two isomers with differences in neutron energy. By contrast, Libby & co-workers (36, 54) have observed that the organic yields of the 18 min. isomer and the 4.4 hr. isomer are the same both in *n*-propyl bromide and *i*-propyl bromide. They point out that if impurities which could react with the inorganic bromine to return it to organic combination were present in the  $C_6H_5Br$  the effect would reduce the apparent retention of the 18 min. species relative to the 4.4 hr. species because of its shorter life time in the solution. In the writer's laboratory it has been found difficult to purify  $C_6H_5Br$  adequately to obtain reproducible organic yields. Capron, Crevecoeur & Faes (112) have observed differences in the ratio of 18 min. to 4.4 hr. activity picked up by charged plates immersed in neutron irradiated  $C_6H_5Br$  and have attributed this to differences in recoil energy of the two isomers. Capron & Verhoeve-Stokkink (113) report that the ratio of bromine isomers and also the ratio of rhodium isomers formed by irradiation of samples at varying distances of paraffin from a Ra-Be source varies significantly in a manner which they ascribe to the existence of different capture levels in the bombarded nuclei.

The yields of activity present as  $MnO_2$  following neutron irradiation of  $KMnO_4$  as the solid or in solution were found by Broda & Rieder (114) and



Rieder (82) to be independent of whether slow or fast neutrons were used. In solution they were, however, dependent on concentration and pH. This is cited as evidence that the stable products are formed by secondary chemical reaction after the nuclear explosion, in contrast to the case of irradiation of arsenites and arsenates (78a) where a higher proportion of the activity was found as As(V) when either type of solid salt was irradiated with fast neutrons rather than slow, while the yield in solution was independent of pH and concentration.

Fox & Libby (36) observed, and Rowland & Libby (54) have investigated further, an isotope effect which is apparent as a higher organic yield of  $\text{Br}^{82}$  than  $\text{Br}^{80m}$  from the irradiation of crystalline organic bromides at  $-196^\circ\text{C}$ . The effect is absent in the liquid and in the case of four alkyl bromide glasses tested at  $-196^\circ$ . The authors rationalize the results in terms of the epithermal reaction hypothesis and conclude that  $\text{Br}^{82}$  must have less recoil energy than  $\text{Br}^{80m}$ .

The yields of  $\text{Sb}^{122}$  and  $\text{Sb}^{124}$  recoverable from neutron irradiated triphenylstibine by aqueous extractants have been found to be equal [Kahn (115)].

#### EFFECTS OF BACKGROUND RADIATION ON REACTIONS ACTIVATED BY NUCLEAR TRANSFORMATIONS

In the study of reactions activated by nuclear processes other than radioactive decay, neutrons or other bombarding particles are used. Most methods of providing such particles also generate  $\gamma$ -rays, and in some cases fast neutrons are present. These radiations may produce ions, free radicals, and excited molecules in the medium. In many studies of the type discussed in this chapter it is essential to know with certainty whether the fate of any of the atoms activated by nuclear transformation is altered by these radiation produced species. In alkyl halides, for example, the organic yield following ( $n, \gamma$ ) activation might be changed if such radicals reacted with either the activated atoms or with their stable products. It has been shown that the probability of the reaction with atoms is negligible because the steady state concentration of radicals maintained in a typical experiment with, for example, a radiation level of 5,000 r/hr. must be of the order of  $10^{-11}$  mole fraction whereas each thermalized recoil atom is present in a volume element of solution containing radicals which it itself has produced at a mole fraction of  $10^{-3}$  (22). Tracer experiments (22, 23, 30) on the rate at which low concentrations of dissolved radiohalogen enter organic combination under intense  $\gamma$ -irradiation have served to show that the reaction of radiation-produced radicals with stable products containing the recoil atoms can not have influenced either the organic yield or such phenomena as the scavenger effect in typical investigations of ( $n, \gamma$ ) activated reactions which have been reported. Various workers have made the observation that with Ra-Be neutron sources, or with pile bombardments of moderate duration wide variations in  $\gamma$ -ray intensity cause no alteration in organic yields



[for example: (22, 36, 38, 42)]. Rowland & Libby (54) have recently reported that the organic yield from n-propyl bromide is identical when irradiated with neutrons from a cyclotron with a gamma flux of 700 r/hr. or neutrons from a 30 curie Po-Be source with 0.1 r/hr. These observations all confirm the conclusion that radiation effects are not important in studies of this type.

It should be recalled, however, that prolonged pile bombardments may cause serious radiation effects in some systems (77, 116) and that the product distribution following ( $n$ ,  $\gamma$ ) activation of certain oxy-anions has been found to be sensitive to  $\gamma$ -radiation (16, 76).

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# SEPARATION TECHNIQUES USED IN RADIOCHEMISTRY<sup>1</sup>

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## INTRODUCTION

Shortly after the discovery of radioactivity by Becquerel (1) in 1896, this phenomenon was shown to be associated with certain chemical elements without regard to their chemical or physical state. Chemical separations were used by the Curies (2, 3) and by Rutherford & Soddy (4) to isolate and identify the elements responsible for the observed radioactivities. Many uses were found for the natural radioelements, particularly radium, and a considerable industry soon grew up. The state of this industry as of 1925 was reviewed by Matignan & Marchal (5). They discussed various applications of radium and the more important radioactive minerals and their treatment. The discovery of nuclear transmutation in 1919 by Rutherford (6) and of artificial radioactivity in 1934 by Curie & Joliot (7) stimulated a great deal of interest in the field. The discovery of uranium fission by Hahn & Strassman (8) in 1939 and its subsequent development for wartime use brought the whole subject before the general public as a field of major practical importance. Standard analytical chemical techniques were employed for exploring the new field and some very powerful new ones were developed specifically for radiochemical use, especially under the Manhattan Project during World War II.

It is the purpose of this article to review some of the major chemical techniques now in general use for the preparation and identification of the hundreds of radioactive species which may now be prepared (9). The comprehensive works in the field of radiochemistry have been considered to be those of Paneth in 1928 (10) and of Hahn in 1936 (11). The many advances made in the field since the time of these writings were reviewed in 1949 by Broda (12). Measurement of radiation and the errors which may arise therefrom will not be discussed. However, a number of references, of which we mention but a few, are available to the experimenter in this field (13, 14, 15, 16). The special problems which arise in the synthesis of organic mole-

<sup>1</sup> The survey of the literature pertaining to this review was concluded in March, 1953.

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cules labeled in specific positions with radioactive carbon atoms have not been covered. The interested reader is referred to the book compiled by Calvin *et al.* (17).

#### BASIC CONCEPTS OF RADIOCHEMICAL SEPARATIONS

Radiochemistry has been defined by Broda (12) as the chemistry of bodies which are detected by their nuclear radiations. Radiochemical separations are essential for the following lines of research: the separation and chemical identification of previously unknown radioactive species, e.g., (18, 19); the isolation of particular nuclides as tracers for investigation of chemical properties, e.g., (20, 21) or radiation characteristics, e.g., (22, 23); and the study of nuclear processes leading to the formation of particular nuclear species, e.g., (8, 24 to 29).

Radiochemical analysis consists of the determination of the number of atoms of a particular radionuclide by a combination of chemical purification and physical measurements. The amounts of radioactive material used in research such as is mentioned above are generally far too small to weigh. Therefore, radiochemical analysis is based on the following principle: a precisely determined quantity of an element is added to a system containing the radionuclide under investigation, and if complete exchange is attained (see below), the radioisotope of this element will be chemically inseparable from those added to the system. Fractional loss of the added element sustained in subsequent chemical purification will be the same as that of the radioisotope under investigation. Redetermination of the amount of the element added to the system present after chemical purification serves to establish the fraction recovered. The atoms added to determine the fraction recovered may be either macro quantities of stable isotopes of the element, usually termed "carrier," or may be radioactive atoms of another isotope of the element, usually termed "tracer." If a carrier is used, the fraction recovered is usually determined by weighing; if tracer is used, the determination is made by measuring the radiations of the added tracer atoms. The only detectable deviations from the principle of chemical inseparability of isotopes of the same element are found among the lightest elements, but even these deviations may be neglected for radiochemical analyses (30, 31, 32).

#### EXCHANGE

In order to prevent separation of the carrier material from the radioactive tracer during the process of purification, the added carrier must be distributed randomly in space and among chemical states in precisely the same manner as the radioisotope to be separated. Ideally, the carrier and tracer should be present in homogeneous solution as a single chemical species.

In many cases, the problem of assuring exchange does not arise. Those elements having one stable oxidation state and chemical species in a given aqueous solution, e.g., the alkali and alkaline earth elements, are considered to exchange rapidly in the absence of complexing agents. Elements having a



number of stable oxidation states may possess one or more species which exchange slowly with other species. For instance, chlorine and chloride ion in acidified aqueous solution undergo an extremely rapid exchange (33). However, there is no appreciable rate of exchange at room temperature between perchlorate ion and chlorate ion, or between perchlorate ion and chlorine or chloride ion in either acid or alkaline solution. Exchange between chlorate ion and chlorine occurs at a measurable rate (34). Other elements possessing nonexchangeable species have been investigated; a number have been listed by Burgus (36). To ensure exchange of all radioisotopes with those of an added carrier, all atoms are usually converted to the same chemical species before any attempt at chemical separation is made. Complete exchange of radioiodine with carrier iodine atoms is achieved by the addition of carrier iodine as iodide and subsequent oxidation to periodate (37, 38).

For a thorough discussion of exchange, the reader is referred to the article by Myers & Prestwood (35, p. 6) and the review article on artificial radioactivity by Seaborg (39).

*Incomplete exchange.*—Exchange may be incomplete in systems to which the carrier is added in insoluble form, since losses may occur if the atoms in solution exchange slowly with those of the solid. This difficulty is most likely to occur if the radioisotope is present in colloidal form. Such colloids are known as radiocolloids (40) and have been observed with a number of elements such as zirconium and niobium (41, 42, 43), and lead, bismuth, and polonium (44).

Incomplete exchange may be encountered if an insufficient amount of a strong complexing agent is added to either the active material or the carrier before the two are mixed, particularly if the bonds of the complex formed are strongly covalent in character. Certain cyanide complex ions of chromium (45) exchange very slowly, if at all, with free chromium cations; if a radioisotope of chromium is allowed to form complex ions with small amounts of cyanide before the carrier is added, exchange will be delayed unless the amount of cyanide is great enough so that the carrier may also be complexed to the same extent.

If the element under investigation can form a volatile chemical species, care must be exercised during solution of the target that none of the volatile substance, carrier or tracer, escapes the dissolving system before exchange is complete. When radiobromine is isolated from target materials requiring slightly elevated temperatures for dissolution, the target is usually dissolved in a still, and the distillate and still rinsings added to the target solution before the separation is carried out (46). A table listing the measured volatility of a number of carrier-free tracers is given in Wahl & Bonner (35).

A phenomenon complicating the study of exchange reactions has been described by Prestwood & Wahl (47). When one is studying the kinetics of exchange reactions, a partial rapid exchange sometimes occurs during the chemical separation of the species under study. This effect has been called "apparent zero-time exchange" and its possibility should be considered in

such studies. For example, Prestwood and Wahl found, while studying the exchange reactions between Tl (I) and Tl (III), that the separation of the two states by the precipitation of thallic hydroxide induced a rapid partial exchange of the order of 50 per cent, while separation by precipitation of thallic bromide, hexachloroplatinate, or chromate resulted in much less induced exchange.

*Hot Atom Chemistry.*—If an irradiation produces a change in chemical combination without changing the atomic number of an atom, and the resultant state of chemical combination does not exchange rapidly with the original form, then the irradiated atoms may be separated and concentrated. Szilard & Chalmers (48) were the first to demonstrate such reactions by concentrating radioiodine from neutron irradiated ethyl iodide.

These investigators found that after the capture of a neutron by an iodine nucleus, the resultant nucleus is in an excited state and decays to the ground state by emission of a  $\gamma$ -ray. The total energy emitted as  $\gamma$ -radiation following the capture process is of the order of 5 to 8 Mev for most nuclear species, a large fraction of which may be emitted in one quantum. The resultant nucleus recoils with an energy of the order of 100 e.v. (generally termed a "hot atom"), an amount of energy more than sufficient to rupture any chemical bond. Szilard and Chalmers have shown that this phenomenon can be used to separate the recoiling atoms from the stable element exposed to the neutron flux, provided that the element is contained in a complex molecule from which simpler forms of the element are chemically separable, and that isotopic exchange does not occur rapidly between the simpler forms and the complex form. Systems are known for many elements (36) which satisfy these requirements well enough to make possible separation of the radioactive atoms relatively free from the isotopic target atoms.

If the upper state of a pair of nuclear isomers emits a  $\gamma$ -ray during transition to the lower state and the  $\gamma$ -ray is internally converted, the resultant energy may be utilized to effect a separation of the nuclear isomers (49). Bond rupture is not attributable to recoil as in the Szilard-Chalmers reaction, but rather to the high state of excitation of the orbital electrons following conversion of the  $\gamma$ -ray. Willard (50) and Fairbrother (51) deduced this mechanism from the fact that isomeric transitions could initiate reactions which could not occur with energies as small as the recoil energy available, while Seaborg, Friedlander & Kennedy (52) showed that bond rupture occurred only when the  $\gamma$ -ray was internally converted.

Extensive reviews on the subject of hot atom chemistry have been published by Edwards & Davies (53) and by Adamson & Williams (54).

#### STANDARDS OF PURITY

The usual concepts of purity are modified for radiochemical application. There are two types of impurities to be considered: (a) those substances which by their chemical effects or by their amount interfere with the measurements to be made; and (b) radioactive substances which may be present

in unweighably small amounts but which interfere with the measurements to be performed on the radiations emitted by the nuclide under investigation. The degree of purity required depends upon the purpose of the experiment as well as upon the techniques and instruments employed.

When the specific activity of a sample is to be determined by weighing a precipitate and then counting the radiations, the choice of a compound to be weighed is governed by the usual considerations of known composition, stability, and freedom from weighable impurities. A sample to be used for tracer studies need only be free from radioactive impurities and from substances which, by their chemical properties, would interfere with the projected experiment; while for radiation studies, for example, beta spectroscopy, alpha counting, or absolute disintegration rate studies, the final sample must be essentially free of macro amounts of matter. If the desired information is only the amount of a particular species present in a mixture, it is often possible to analyze the decay of radiation intensity with time in such a way that the amount of a particular species may be determined unambiguously. Radioactive impurities with half-lives similar to that of the nuclide under investigation may be tolerated if the counting method detects unambiguously the nuclide to be studied. The care taken to eliminate a particular radioisotope from the sample depends upon the amount of this nuclide present in the original material relative to that of the desired species, the past history of the source material, and possible nuclear reactions involved. For example, if radiocadmium is to be separated from  $U^{235}$  irradiated with thermal neutrons, greater purification from molybdenum activities is required than if the target material is bismuth bombarded with high energy deuterons, because, in the first case, the relative yield of cadmium is very low with respect to that of molybdenum (26), while in the second case it is high (25).

#### SEPARATION TECHNIQUES

When a carrier is used in the isolation of a radionuclide, the initial, complete exchange of the radioisotope with the carrier is essential. The next operation is usually designed to remove gross chemical contamination such as target material or large amounts of reagents. Subsequent steps are in general designed to separate from specific groups of likely impurities. The number and type of steps depend upon the chemical nature of the element to be separated as well as the nature of the impurities to be eliminated. It is frequently necessary to repeat particular separations in order to attain the desired purity; however, it has been found that repeating a step several times generally gives less purification than repeating a cycle of several consecutive different steps. The final step is the preparation in a form suitable for gravimetric determination of the amount of the element recovered after radiochemical purification. It is not necessary that the final step separate from radioactive impurities.

In many experiments it is advantageous or necessary to isolate the radio-

nuclide under investigation free of carrier. Although the chemical properties of carrier-free radionuclides are identical with those of macroscopic quantities of the same elements, the minute quantities of the element necessitate unusual precautions to prevent partial or total loss during chemical separation. Precautions must be taken, for instance, against radiocolloid formation (40, 41, 42, 43, 44) or against adsorption of the tracer on the apparatus (55, 56). Garrison & Hamilton (57) have reviewed a number of methods for the production and isolation of carrier-free radioisotopes.

*Precipitation.*—Group or specific precipitations are frequently used to effect separations. Even in the case where a carrier is not used, it is often possible to precipitate a compound which carries the desired activity and which may later be eliminated by subsequent chemical separation (58 to 62). Hahn had proposed a classification of the types of coprecipitation and non-isotopic carrying. These are: (a) Isomorphous replacement. The tracer is incorporated into the crystal lattice, presumably isomorphously, since a macro amount of the tracer compound will form isomorphous mixed crystals with the carrier compound. (b) Adsorption. The tracer is adsorbed on the surface of the precipitate. (c) Anomalous-Mixed-Crystal-Formation. The tracer is apparently incorporated homogeneously into the carrier crystal lattice, even though in macro amounts it would not form a mixed crystal with the carrier compound. (d) Internal Adsorption. The tracer is apparently adsorbed on the surfaces of growing crystals and becomes trapped, resulting in a non-homogeneous distribution of the tracer within the carrier compound.

Bonner & Kahn (63) state that adsorption is likely to occur if the tracer forms a slightly soluble or slightly dissociated compound with the ion which remains in excess after a precipitation occurs.

Occasionally, when a carrier is used, a precipitation of the carrier which is intended to separate from a particular radio impurity is not effective when the impurity is present in only trace concentrations. Some elements carry as traces by mechanisms *b*, *c*, or *d* above, under conditions in which they are not precipitated when present as macroscopic components (64, 65, 66). The efficacy of the separation in cases such as these may be increased by adding a small amount of inactive material isotopic with the impurity before the precipitation. This "holdback agent," being in vast excess, reduces the concentration of the radioactive impurity in the precipitate.

Group precipitations have often been used to remove impurities. These are known as "scavenge" precipitations. Typical scavenge precipitates are: ferric hydroxide precipitated with ammonia; mixed palladium, antimony, and tellurium sulfides precipitated from hydrochloric acid; and manganese dioxide precipitated from nitric acid. Scavenging by precipitation from homogeneous solution has been found more effective in removing radioactive impurities than carrying by preformed precipitates, for example, the carrying of niobium on manganese dioxide (66). While they are useful in experiments using carrier, scavenges are often incompatible with the isolation of a carrier-free radioisotope.

*Solvent Extraction.*—A powerful separation technique, usually applicable

to both carrier-free and macro amounts of material, is that of solvent extraction (67, 68, 69). Certain compounds of some elements are, under the proper conditions in the aqueous phase, preferentially soluble in immiscible organic solvents. Some solvent extraction processes are highly specific, for example, the extraction of uranyl nitrate from 1 *M* nitric acid—2 *M* calcium nitrate solution into diethyl ether (70), and the extraction of tantalum into diisopropyl ketone from sulfuric acid solutions containing a small amount of fluoride (71). An interesting type of solvent extraction, chelation, has been studied by Calvin & Reid (72, 73), and by Connick & McVey (55) in which zirconium in aqueous solution is complexed by thenoyltrifluoroacetone in benzene solution, the complex being preferentially soluble in benzene.

It is usually possible to alter the conditions of the solvent extraction system so that the desired element passes back into the aqueous phase. This "back extraction" may act further to increase the specificity of the solvent extraction operation as well as to return the substance under investigation to a more convenient medium for further purification. For example, niobium may be extracted into diisopropyl ketone from 10 *M* hydrochloric acid, together with Mo (VI), Fe (III), Ga, Sb (V), In, Tl (III), Au (III) Te (VI) and Se (VI) and probably small amounts of other elements (74); of this group, only niobium is back-extracted quantitatively into 6 *M* hydrochloric acid, while of the others, only Mo (VI) and In back-extract to any appreciable extent.

Some difficulties may arise in solvent-extraction such as emulsion formation or the slow attainment of equilibrium. For example, the rate of extraction of zirconium into a solution of thenoyltrifluoroacetone in benzene depends upon the rate of formation of the complex at the interface (55). The organic phase may extract enough of the reagents from the aqueous phase to alter the original conditions of extraction. The extraction of gallium from hydrochloric acid by diethyl ether, for example, is extremely sensitive to acid concentration (75) and the solubility of hydrochloric acid in ether is well known. There may be a tendency for radiocolloidal impurities, not in themselves extractable, to collect on the interface between the phases (40). Substances which extract in macro amounts may not extract as readily in trace quantities. Tripositive iron extracts well into diethyl ether from 6 *M* hydrochloric acid in macroscopic quantities, but extracts much less readily in trace amounts (76).

*Ion Exchange.*—The development during the last fifteen years of synthetic ion-exchange resins has presented the radiochemist with a generally applicable separation technique, the only one so far known which is invariably as useful for carrier-free separations as for those employing carriers. An ion-exchange resin is an organic polymer with groups attached which make hydrogen or hydroxyl ions easily available by ionization (77). It has been shown by Bauman & Eichorn (78), that the solid ion-exchange resin may be considered equivalent to a highly ionized salt solution through which ions can diffuse. The manner in which an ionic species distributes itself at equilibrium between the resin and the surrounding solution under any given



set of conditions is characteristic of the ionic species; almost any two species will show some difference in distribution under properly selected conditions and may be separated by successive adsorption and desorption. Usually, a long column of resin is prepared, at the top of which is placed a very thin band of adsorbed ions to be separated. An eluting solution is passed slowly through the column to provide equilibrium conditions in which the differences in distribution coefficients of the ions to be separated are as large as possible. An ion with a given distribution coefficient will move more slowly on the column bed than will an ion which has a lower distribution coefficient, so that different ions will flow down the column at different rates and will appear in the eluates at different times. This successive adsorption and desorption of ions utilizes differences of distribution coefficients in such a way that elements with very similar adsorption equilibria may be separated. Marinsky, Glendenin & Coryell first isolated element 61 from other rare earth fission products by ion exchange techniques (79).

The separation of rare earths by the use of ion-exchange resin columns was developed in the Manhattan Project and has been described in a comprehensive series of papers (80, 81, 82). This differential elution technique has been described in detail by Wilkinson & Hicks (83) and a mathematical analysis of ion exchange has been given by Boyd, Schubert & Adamson (84). Column separation techniques have been applied to the separation of the lanthanides (85), the alkaline earths (86), and the hafnium-zirconium pair (87); they have been the key to the discovery of the newer transuranium elements (88, 89).

These resins may also be used to separate different ionic species; for example, if an element forms a negatively charged complex with chloride ion under certain conditions, the ion will be adsorbed on a column of anion exchange resin. All cationic and uncharged species will pass through the column. The concentration of chloride ion in the eluting agent is then changed in such a manner that the dominant species of the adsorbed element in solution is no longer anionic, and the element is eluted rapidly.

Separations have been carried out using adsorbents other than an ion exchange resin. One adsorbs the element on paper (90), for instance, and elutes with one or more suitable media to separate various elements. A number of elements have been successfully separated using this technique of paper chromatography, although the small capacity of the paper (up to 300  $\mu\text{gm.}$ ) limits the applicability of the method with respect to the usual radiochemical analysis with carrier. Zirconium and hafnium have been separated by adsorption of the chlorides on columns of silica gel from anhydrous methanol and subsequent differential elution (91).

*Distillation.*—Distillation techniques have occasionally been applied to inorganic radiochemical separations. A small group of elements form volatile halogen compounds under various conditions, and four elements (ruthenium, osmium, technetium, and rhenium) have oxides sufficiently volatile to be distilled. The noble gases, halogens and mercury may be distilled as the



elements. As an aid in transferring the small amounts of material customarily separated, the vapors are usually swept through the apparatus with a stream of gas and trapped in some suitable medium. Distillations are very useful as preliminary separation steps since they are generally satisfactory for separating from macro amounts of nonvolatile impurities. Distillation separations for ruthenium (92), germanium and arsenic (93), selenium (94), bromine (95), technetium (96), antimony (97), osmium (98), astatine (99), rhenium (100), francium (101), and polonium (102) have been reported by many authors. Gaseous products of nuclear reactions have been separated by volatilization, this technique being particularly useful for the identification of noble gas fission products (103 to 109).

*Electrochemical methods.*—Electrochemical methods, both chemical and electrolytic deposition, have been applied to systems containing radionuclides. Hevesy & Paneth (110) showed that electrodeposition of tracer quantities obeyed the same laws as macro quantities of the same element. Haïssinsky (111) confirmed the early results with the  $\text{Bi}^0$ -Bi (III) system and showed that bismuth obeyed Nernst's equation in concentrations as low as  $10^{-12}$  N. Other elements, however, do not always obey Nernst's equation, for example, polonium (112, 113) and zinc (114). In some cases, chemical plating of trace amounts of metals does not follow the behavior predicted from the oxidation potentials of the elements; for instance, silver will plate on gold or platinum (115). The mechanism of this anomalous chemical plating behavior has been considered to involve diffusion of the ion into the metal and subsequent exchange. Chemical plating methods have been employed to deposit carrier-free radionuclides of a number of elements, e.g., polonium on silver (110), of bismuth on nickel (110), and of copper on lead (116). Electrolytic depositions of radionuclides of many elements have been exploited, e.g., iron (117), copper (118), technetium (119), cadmium (120), and indium (121). Haïssinsky (122) has reviewed the preparative as well as the theoretical aspect of this phase of radiochemistry.

In some cases (123), the degree of purification obtained by electrochemical methods is not large; however, for the preparation of counting samples these methods are unexcelled. When the radionuclide is to be isolated with carrier, electroplating of the element results in a uniformly-thick deposit which simplifies correction of counting data due to effects of the sample itself.

#### SUMMARY

We have endeavored to discuss some of the major techniques now in common use in radiochemistry. Readers interested in learning further details of technique, and the applications of radiochemical methods to the investigation of nuclear processes, the analysis of trace impurities and the like, will find many excellent books and articles in the field, some of which we cite (124 to 132). A number of useful general references are also included (133 to 140).

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# ISOTOPE EFFECTS IN CHEMICAL REACTIONS<sup>1</sup>

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## INTRODUCTORY NOTE

This review is intended to summarize progress reported during the calendar year 1952 in investigations of the effect of isotopic substitution on the rates and equilibria of chemical reactions. A number of references to reports of Government-sponsored research projects have been omitted because the reviewer felt that this summary would be most useful if the literature citations were limited to standard periodicals or books likely to be available immediately in most libraries connected with scientific institutions. Nearly all unclassified project research is published eventually in the open literature.

## ISOTOPES OF HYDROGEN

In a study on the kinetics and mechanisms related to acid catalysis, Roberts, Regan & Allen (1) measured the rates of reaction of diphenyldiazomethane with benzoic acid and ethyl diazoacetate with *p*-toluenesulfonic acid in  $C_2H_5OH$  or  $C_2H_5OD$ . At 30°C. the ratio of specific rate constants  $k_H/k_D$  is 3.62 for the former pair and 0.55 for the latter. The enhancement of the rate of reaction of ethyl diazoacetate in  $C_2H_5OD$  as compared with that in  $C_2H_5OH$  is regarded as an indication of the "operation of a substrate-catalyst equilibrium before the rate determining step".

Roberts & Regan (2) studied the rates of reaction of  $CH_3COOH$  and  $CD_3COOD$  with diphenyldiazomethane in ethanol solutions. The rates of reaction of the isotopic acetic acids were closely the same in all cases, but the absolute rate of reaction depended upon the deuterium content of the solvent. At 30°C. the relative rates of reaction in 82.5 volume per cent  $C_2H_5OH$  plus 17.5 per cent  $H_2O$  were the same but with  $D_2O$ , and 100 per cent  $C_2H_5OD$  were 13.5, 8.0 and 1.0, respectively. The rate of reaction of acetic acid in  $C_2H_5OH$  was 3.5 times that in  $C_2H_5OD$ ; this effect of a rate-determining proton transfer is to be compared with the rate constant ratio of 3.6 observed in the corresponding system with benzoic acid (1).

Cohen & Westheimer (3) have found that the relative rates of oxidation of  $CH_3CDOHCH_3$  and  $CD_3CHOHCD_3$ , compared with that of  $CH_3CHOHCH_3$ , are the same in 86.5 weight per cent acetic acid solution as in water (4). Near 0°C.  $k_H/k_D$  is about 8 for the oxidation of  $CH_3CDOHCH_3$  with  $HCrO_4^-$  compared with that of  $CH_3CHOHCH_3$ ; this rate constant ratio is only 1.1 for the comparison of the oxidation of  $CH_3CHOHCH_3$  and  $CD_3CHOHCD_3$ .

<sup>1</sup> The survey of the literature pertaining to this review was concluded in March, 1953.

Leo & Westheimer (5) have found that in dry benzene, and in the presence of excess  $\text{CH}_3\text{CDOHCH}_3$ , the rate of decomposition of the chromic acid ester of  $\text{CH}_3\text{CDOHCH}_3$  is about 1/5.2 to 1/4 that of the ester of ordinary isopropyl alcohol. When the alcohol-free ester of the deuterioalcohol is decomposed by pyridine in wet benzene, the rate of hydrolysis is nearly the same as for the ester of ordinary isopropyl alcohol.

Shiner (6) has determined the rates of the bimolecular substitution and elimination reactions in alcoholic  $\text{C}_2\text{H}_5\text{ONa}$  of  $\text{CH}_3\text{CHBrCH}_2\text{D}$  and  $\text{CD}_3\text{CHBrCH}_3$  compared with those of  $\text{CH}_3\text{CHBrCH}_3$ . The rates of substitution are the same for all three compounds, while the rate of elimination of  $\text{CD}_3\text{CHBrCD}_3$  is only 1/6.7 that of the other two. It is concluded that these results are in accord with predictions of  $\text{S}_{\text{N}}2$  and  $\text{E}2$  mechanisms.

In an attempt to test the applicability of either the Neunhoeffer-Paschke (7) or Bell-Reed (8) mechanism to the thermal decomposition of carboxylic acid salts, Wiberg (9) investigated the pyrolysis of a mixture of deuterated and undeuterated barium butyrate. Exchange between the two was found to be rapid with respect to the rate of decomposition, a result in accord with, but not conclusive evidence for, the Neunhoeffer-Paschke mechanism. The data obtained permit the calculation of the equilibrium constant for the exchange reaction among the deuterated and undeuterated species of butyrate ion. For the reaction written  $\text{ion-d}_2 + \text{ion-d}_0 = 2 \text{ ion-d}_1$ ,  $K = 3.4 \pm 0.2$  at  $365^\circ\text{C}$ .

Kaplan & Wilzbach (10) have repeated the experiments of Gilman, Dunn & Hammond (11) on the relative rates of hydrolysis in moist piperidine of hydrogen-isotopic triphenyl silane. The result of the earlier study was that triphenylsilane-d reacted about 6 times as fast as its protium analog. Kaplan & Wilzbach employed tritium labeled material and found  $k_{\text{T}}/k_{\text{H}} = 0.796 \pm 0.004$ , which was in the direction expected from theory; a value of 0.8 for the ratio was calculated considering only the stretching frequencies of the Si—H and H—H bonds in the normal molecules and an assumed linear activated complex. Similar results were obtained on the alkaline alcoholic hydrolysis of tripropylsilane-t and ordinary tripropylsilane.

Majury & Steacie (12) investigated the reactions with  $\text{H}_2$  and  $\text{D}_2$  of  $\text{CH}_3$  and  $\text{CD}_3$  radicals produced by the photolysis of acetone. The effects of substitution of D for H in each species can be seen from the following rate constant ratios:  $(\text{CH}_3 + \text{H}_2)/(\text{CH}_3 + \text{D}_2) = 3.3$ ,  $(\text{CD}_3 + \text{H}_2)/(\text{CD}_3 + \text{D}_2) = 3.5$ ,  $(\text{CH}_3 + \text{H}_2)/(\text{CD}_3 + \text{H}_2) = 0.71$  and  $(\text{CH}_3 + \text{D}_2)/(\text{CD}_3 + \text{D}_2) = 0.74$ . The following energies of activation were found:  $\text{CH}_3$  (or  $\text{CD}_3$ ) +  $\text{H}_2$ ,  $9.7 \pm 0.6$  kcal.;  $\text{CH}_3$  (or  $\text{CD}_3$ ) +  $\text{D}_2$ ,  $11.3 \pm 0.6$  kcal. Davison & Burton (13) conducted a similar research and concluded that the activation energy for  $\text{CH}_3 + \text{H}_2$  should be greater than 13 kcal.

Weston & Bigeleisen (14) have measured the exchange equilibrium of H and D between liquid water and gaseous phosphine. For the reaction written  $\text{PH}_2\text{D} + \text{H}_2\text{O} = \text{PH}_3 + \text{HDO}$ , all substances gaseous, a value of 1.52 at  $25^\circ\text{C}$ . is calculated for K by use of the ratio of vapor pressures of  $\text{H}_2\text{O}$  and  $\text{HDO}$ . Using a calculated difference in the zero point energies of  $\text{PH}_3$  and  $\text{PH}_2\text{D}$ ,

the authors find the relation for the gaseous reaction  $K = 0.781 \exp(198/T)$  to be valid up to about 500°K.

Matraw, Pachucki & Dorfman (15) have investigated the  $H_2$ - $T_2$  equilibrium mass spectrometrically. At 28°C. the constant for the isotopic equilibrium induced by the  $\beta$ -radiation from tritium decay is given by  $(HT)^2/(H_2 \cdot T_2) = 2.87 \pm 0.6$ ; a value of 2.57 has been calculated for 25°C. (16). The authors suggest two possibilities in explanation of the high experimental value: a higher effective temperature in the electron beam of the mass spectrometer than expected, or a difference in the state of equilibrium in a radiation field.

Bond, Sheridan & Whiffen (17) determined the rate of approach to equilibrium and the state of equilibrium in the reaction  $C_2H_2 + C_2D_2 = 2C_2HD$  between 60 and 119°C. over a Ni catalyst; an infrared absorption method was employed. Rather erratic values for the equilibrium constant were found and the data over the whole temperature range were expressed as  $K = 3.2 \pm 0.2$ . A revision of the calculation of Glockler & Morrell (18) yields a mean value of about 3.6 (with an uncertainty of perhaps 0.3) over this temperature range.

In a study involving similar analytical methods, Stedman (19) has investigated the disproportionation of deuterated ammonia. The symmetrical end members of the set of isotopic isomers  $ND_3$  and  $NH_3$  appeared to be present in concentrations greater than those predicted by statistical calculation. These measurements have been criticized by Bigeleisen (20) who concluded that the results obtained by Stedman were subject to rather larger experimental errors than those for which allowance was made.

Eidinoff *et al.* (21) measured the equilibrium between H, D and T in the system: hydrogen-acetic acid. The isotopically equilibrated hydrogenation system was used in the presence of Pt catalyst to saturate the double bond in methyl-3- $\alpha$ -acetoxy- $\Delta^{11}$ -cholenate. The isotopic composition of the atoms incorporated during the hydrogenation was measured relative to that of the carboxyl hydrogen of the acetic acid medium and to that of the hydrogen gas. The former comparison indicated that exchange between dissolved and carboxyl hydrogen at the catalyst surface is rapid relative to the rate of hydrogenation; the latter comparison indicated preferential uptake of D by a factor of 1.10 and T by a factor of 1.26 relative to H. These findings indicate relatively loose binding of the hydrogen atoms at the catalyst surface.

A number of experiments on relative rates of hydrogen isotope reactions have been carried out on systems of biochemical interest. Thorn (22) measured the isotope effect in the oxidation of deuteriosuccinic acids in the presence of the succinic acid oxidase system. The relative rates of oxidation of the methylene- $d_0$ ,  $-d_2$  and  $-d_4$  compounds were found to be 2.5, 1.8 and 1.0, respectively. The energies of activation were measured for the reactions of the methylene- $d_0$  and  $-d_4$  compounds and were  $11,250 \pm 150$  and  $12,700 \pm 300$  cal., respectively. Verly *et al.* (23) determined the isotopic contents of the

methyl groups of choline and creatine isolated from the tissues of rats administered a mixture of methanols containing  $C^{14}$ ,  $D$  and  $T$ . These isotope contents were compared with those of the methanol administered. The ratio of  $D$  to  $C^{14}$  in the choline methyl group was 22 per cent of that in the methanol, whereas the  $T/C^{14}$  ratio was 69 to 75 per cent of that in the methanol. The interpretation of the biological pathways of the methanol might thus depend upon whether  $T$  or  $D$  was used as label. Glascock & Dunscombe (24) established, by feeding, a body water level of 2.5 per cent  $D_2O$  and 1 microcurie per ml. of HTO in lactating nursing rats. Relative to  $T/D=1$  for body water, fatty acids isolated from various tissues all had  $T/D$  less than unity; the lowest value, 0.8, was found with the mammary gland fatty acids, and a somewhat higher value was observed for liver fatty acids.

In a general paper on the significance of isotopic reactions in rate theory, Eyring & Cagle (25) have treated a number of reactions involving hydrogen. The electrolysis of water is studied in terms of the differences in rate attributable to the effect of isotope substitution on the O-H stretching frequency in water, and the two-mechanism character of the process is discussed. The very large isotope effect in the reaction of water and aluminum carbide to yield methane is also analyzed.

#### ISOTOPES OF CARBON

A summary of work done on carbon isotope effects to late Autumn 1952 is given by Ropp (26); the review contains a number of references to unpublished experimentation.

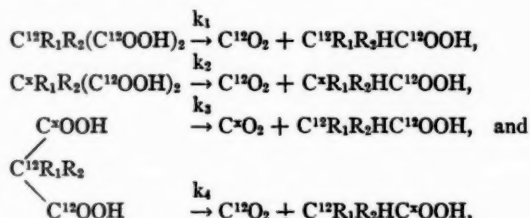
Baertschi (27) has measured the fractionation of carbon isotope incident upon the absorption of  $CO_2$  by aqueous  $Ba(OH)_2$ . A fractionation factor of 1.014 for  $C^{12}O_2$  relative to  $C^{13}O_2$  was observed on absorption from a gas stream which was 2.6 per cent  $CO_2$  and 97.4 per cent  $N_2$ . The factor was 1.011 for a pure  $CO_2$  stream. These results are what would be expected, since there is a greater diffusion effect in the case of absorption from a stream of diluted  $CO_2$ .

Stranks & Harris (28) determined the equilibrium constant for the reaction  $Co(NH_3)_4C^{12}O_3^{+} + (HC^{14}O_3^{-} + C^{14}O_3^{-}) = Co(NH_3)_4C^{14}O_3^{+} + (HC^{12}O_3^{-} + C^{12}O_3^{-})$  in the temperature range  $0^{\circ}$  to  $30^{\circ}$  C.;  $K$  values found ranged from  $0.875 \pm 0.002$  at the lower temperature to  $0.900 \pm 0.004$  at the higher. Measurement of this isotope effect was carried out in conjunction with the determination of the kinetics and mechanism of the above reaction (29). It is interesting to compare these results with those of Yankwich & McNamara (30), who measured the relative rates of approach to equilibrium and the equilibrium constants for  $C^{13}$  and  $C^{14}$  exchange in the similar bis-ethylenediamine ligand system. The equilibrium constants, for reaction written as above, were  $0.991 \pm 0.014$  for  $C^{13}$  exchange and  $0.990 \pm 0.019$  for  $C^{14}$  exchange. The rate constant ratio  $k_{13}/k_{14}$  was determined to be  $1.033 \pm 0.028$ .

Stranks & Harris (28) also studied the isotope effect in the acidic decom-

position of the carbonatotetraamine complex ion and found it to be insignificant.

A number of studies were published in 1952 of the isotope effects in the decarboxylation of malonic acids. For convenience, the notation of Bigeleisen & Friedman (31) will be given here.



where  $x$  is 13 or 14.

Lindsay, Bourns & Thode (32) measured  $k_1/2k_3$  for  $x=13$  between 137° and 196°C. They found no apparent variation with temperature and report a value  $1.036 \pm 0.003$ . This result was obtained with BDH (British Drug House) malonic acid and is to be compared with earlier values obtained near the melting point of 135°C. with Eastman Kodak malonic acid: Lindsay, Bourns & Thode (33) found 1.046 in a single experiment, while Bigeleisen & Friedman (31) found  $1.037 \pm 0.002$  in two experiments. The earlier work of Lindsay, Bourns & Thode (33) demonstrated a difference in  $k_4/k_3$  obtained from the two brands of acid. These results must not be regarded as indicative of invariance with temperature of  $k_1/2k_3$ ; the experimental technique employed involved collection of the first one per cent or so of  $\text{CO}_2$  evolved, and under these conditions the temperature of the malonic acid is virtually that of the melting point irrespective of the bath temperature since melting is only a few fold more rapid than decarboxylation in the case of the pure solid acid.

Yankwich, Stivers & Nystrom (34) reported preliminary results of simultaneous determinations of  $k_4/k_3$  for  $\text{C}^{13}$  and  $\text{C}^{14}$  labeling of malonic acid. For  $\text{C}^{13}$  labeling they found 1.026 at 138°C., and for  $\text{C}^{14}$  labeling 1.10 at the same temperature. The  $\text{C}^{14}$  results are in fair agreement with the original report of Yankwich & Calvin (35), but are not at all in accord with the predictions of Bigeleisen (36). The  $\text{C}^{13}$  results agree with those of Lindsay, Bourns & Thode (33), are higher but of the same magnitude as those of Bigeleisen & Friedman (31), and approximate the predictions of theory.

In the course of the test of a treatment of the enrichment of isotopes by differences in rates for irreversible isotopic reactions, Bernstein (37) found 1.033 at about 160°C. for  $k_4/k_3$  for  $\text{C}^{13}$  labeling. The prediction of theory (36) is quite clear for  $k_4/k_3$ , the value being 1.0198 for  $\text{C}^{13}$  labeling and invariant with temperature. The experimental results range from 1.020 (31), through 1.026 (33,34), to 1.033 (37). This should not be considered good agreement with the theory.



Ropp & Raaen (38) prepared malonic acid-2- $C^{14}$  and measured the values of several specific rate constant ratios. For decarboxylation at  $154^{\circ}\text{C}$ . they found  $k_1/k_2=1.076$ ,  $k_1/2k_3=1.065$ , and  $2k_3/k_2=1.01$ . These values depend somewhat on the choice of that for  $k_4/k_3$ .

Fry & Calvin (39) determined  $k_4/k_3$  for  $C^{14}$  labeling with  $\alpha$ -naphthyl- and phenylmalonic acids in the melt and in dioxane-1 *N* HCl solution. For the naphthylmalonic acid  $k_4/k_3$  was  $1.076 \pm 0.005$  in the melt at  $163^{\circ}\text{C}$ . and  $1.097 \pm 0.011$  in solution between  $73^{\circ}$  and  $88^{\circ}\text{C}$ . For phenylmalonic acid the corresponding figures are  $1.088 \pm 0.018$  and  $1.132 \pm 0.017$ . In all cases the results are higher than those predicted (36). Even though the average deviations of the above results are large, they are not inconclusive evidence for a solvent and/or temperature effect on the value of  $k_4/k_3$ .

One of the most important results of the work on the carbon isotope effects in malonic acid decarboxylation is that the presently available data indicate a ratio of  $C^{14}$  to  $C^{13}$  effects which is larger than the value 2 predicted by theory. Two papers other than (34) appeared during 1952 which bear on this problem.

Stevens, Pepper & Lounsbury (40) repeated at  $60^{\circ}\text{C}$ . with  $C^{13}$  and  $C^{14}$  labeled mesitoic acid the decarboxylation experiments of Bothner-By & Bigeleisen (41). The medium employed, 86 per cent aqueous  $\text{H}_2\text{SO}_4$ , was the same as in the earlier work as was the method of isotope analysis, mass spectrometry, for both tracer nuclides. The results were  $k_{12}/k_{13}=1.038 \pm 0.001$  (Bothner-By & Bigeleisen obtained  $1.036 \pm 0.003$ ), and  $k_{12}/k_{14}=1.101 \pm 0.007$ . The ratio of isotope effects is  $2.8 \pm 0.3$  for these experiments as compared with 2.00 predicted by theory (36).

Schmitt, Myerson & Daniels (42) have repeated the earlier work of Daniels & Myerson (43) on the relative rates of enzymatic hydrolysis of  $C^{14}$  and  $C^{13}$  labeled urea. Both tracer nuclides were determined mass spectrometrically, and the results were  $k_{12}/k_{13}=1.010 \pm 0.001$  and  $k_{12}/k_{14}=1.032 \pm 0.002$ . The ratio of the isotope effects is  $3.2 \pm 0.4$ , and both are much smaller than values predicted on the basis of the rupture of a C—N bond as the rate-determining step. These workers are studying the same reaction under nonenzymatic conditions.

While there is strong indication that in certain reactions the ratio of  $C^{14}$  to  $C^{13}$  isotope effects is greater than 2, considerable and more accurate data will need to be presented before many physical chemists are willing to admit the validity of this observation as a crucial test of the absolute reaction rate theory.

Bernstein (37) measured the  $C^{13}$  isotope effect in the pyrolysis of  $\text{Ni}(\text{CO})_4$  in a flow system at a mean temperature, for two experiments, of  $112^{\circ}\text{C}$ . The relative rates of production of  $C^{12}\text{O}$  and  $C^{13}\text{O}$ ,  $k_{12}/4k_{13}$ , was found to be 1.059.

Stevens, Pepper & Lounsbury (44) searched for a  $C^{13}$  isotope effect in the decarboxylation of anthranilic acid,  $o\text{-NH}_2\text{C}_6\text{H}_4\text{COOH}$ , and found none.



Using the Schenkel & Schenkel-Rudin mechanism (45) as a starting point, the authors conclude that the mechanism of the decarboxylation is best explained as a bimolecular electrophilic substitution, with the attack of a proton being the rate-determining step. Proton attack on the  $\alpha$ -carbon of the zwitterion is the detailed mechanism considered most likely.

Fry & Calvin (46) have investigated the  $C^{13}$  and  $C^{14}$  isotope effects in the decarboxylation of oxalic acid in 100 per cent  $H_2SO_4$  solution. The notation given above for malonic acid can be used to summarize their results. At  $103^\circ C$ ,  $k_4/k_3$  is  $1.027 \pm 0.002$  for  $C^{13}$  label and  $1.055 \pm 0.003$  for  $C^{14}$ ; at  $80^\circ C$ , the corresponding values are  $1.033 \pm 0.002$  and  $1.067 \pm 0.004$ . The results obtained at the higher temperature are in agreement with the value  $1.032 \pm 0.007$  given earlier by Lindsay, McElcheran & Thode (47). These isotope effects are larger than those predicted by the treatment of Bigeleisen and show an effect of temperature which the theory does not admit. Fry and Calvin have obtained good general agreement with the experimental results by assuming a somewhat different model for the activated complex and considering the effect of possible equilibria of an acid-base type antecedent to the rate-determining step. Bigeleisen, in the printed discussion of this paper, has made valid criticism of certain features of the calculation. It is interesting to note that the ratio of  $C^{14}$  to  $C^{13}$  isotope effects in these experiments is  $2.0 \pm 0.2$  at both temperatures, in agreement with prediction (36).

Ropp & Raaen (48) have made a very interesting contribution in measuring the effect of nuclear substituents on the  $C^{14}$  isotope effect in the saponification of various ethyl benzoates at  $25^\circ C$ . The values of  $k_{12}/k_{14}$  and Hammett's  $\sigma$  for each substituent (49) are: *p*- $OCH_3$ , 1.091 ( $-0.268$ ); *p*-Cl, 1.081 ( $+0.227$ ); *p*- $CH_3$ , 1.078 ( $-0.170$ ); none, 1.077; *m*-Cl, 1.072 ( $+0.373$ ); *m*- $NO_2$ , 1.067 ( $+0.710$ ). Within limits of error somewhat larger than those given by the authors, there is general correspondence between the  $\sigma$  and  $k_{12}/k_{14}$  values. The effect of substituent groups has not been incorporated into models designed to explain the isotope effects observed in reactions of this type, but it seems reasonable that there should be some correlation between the isotope effects observed and the effect of the substituent as determined from similar kinetic studies.

Downes & Harris (50) have investigated the isotope effect in a reaction as determined by measurements on the unreacted substance compared with the more general method of isotope analyses on the products. They studied the Cannizzaro reaction on  $C^{14}$ -labeled  $HCHO$  at  $60^\circ C$ . Unreacted formaldehyde was precipitated from aliquots of the reaction mixture with dimedone or 2,4-dinitrophenylhydrazine; the solid was washed and recrystallized, then counted with an end-window GM tube. The value found for  $k_{12}/k_{14}$  was  $1.060 \pm 0.001$ .

Brown & Holland (51) have measured the  $C^{14}$  isotope effect in the reaction of carbonyl-labeled benzophenone with 2,4-dinitrophenylhydrazine. The specific activities of the original ketone and the phenylhydrazone were

compared after about 10 per cent reaction. The authors give  $k_{12}/k_{14}=1.099 \pm 0.011$  at  $27.8^\circ\text{C}$ . This result is obtained by averaging the primary data, a procedure which is not proper for the situation in which various runs represent different degrees of reaction. Averaging of the directly calculated rate constant ratios gives  $k_{12}/k_{14}=1.097 \pm 0.020$ ; the mean deviation in this figure is more nearly what one would expect for data obtained by solid counting.

Roe & Albenesius (52) have measured the  $\text{C}^{14}$  isotope effect in the iodination of methyl-labeled acetone. The reaction was allowed to approach completion and the specific activities of the iodoform and acetate produced were compared with that of the original acetone. In the notation used above for malonic acid, with the carboxyl groups replaced by methyls and  $\text{CO}_2$  taken as  $\text{CHI}_3$ ,  $k_3/k_4=1.056 \pm 0.006$  (wet combustion of samples) or  $1.036 \pm 0.004$  (dry combustions). This isotope effect is apparently in a direction the reverse of those commonly observed. The results given above were recalculated by the reviewer from the counting data given by the authors; they are based on the specific activities of the acetone and iodoform, these being more precise than that of the acetate. The dry combustion results are to be preferred to those obtained by wet combustion (53). The rate determining step in this reaction is known to be the removal of a proton, and that methyl group from which the proton is removed becomes  $\text{CHI}_3$ . Proton removal from the  $\text{C}^{14}$  methyl is not favored; examination of the formation of the carbanion in terms of Bigeleisen's application (54) of the theory of absolute reaction rates shows that the reduced mass term for proton removal as the rate-determining step is 0.994 for  $k_3/k_4$ . The "reversal" of the isotope effect is therefore, attributable to the terms in the free energy factor. Of these, that attributable to isotopic substitution in the normal molecules can be set equal to zero, since the species whose reaction rates are being compared are identical; only the term attributable to isotopic substitution effects in the activated complexes remains. Because of the assumption of negative charge incident to activation, there is a pronounced change in the nature of bonding about the attacked carbon atom and the free energy factor term for the activated complexes is greater than zero; this results in  $k_4/k_3$  being less than one, with  $k_3/k_4$  being greater.

Roe & Finlay (55) searched for a  $\text{C}^{14}$  isotope effect in the pyrolysis at  $490^\circ\text{C}$ . of carboxyl-labeled lithium acetate. The following relative millimolar specific activities were observed:  $\text{CH}_3\text{COOLi}$ ,  $49.1 \pm 0.1$  (20 determinations);  $\text{CH}_3\text{COCH}_3$ ,  $49.0 \pm 0.1$  (9);  $\text{Li}_2\text{CO}_3$ ,  $48.2 \pm 0.1$  (16). Taken as they stand, these results indicate no isotope effect, but the combination of the primary data for many different runs makes it impossible to judge the limit within which the magnitude of the effect or its lack of magnitude has been determined.

In a study of the pyrolysis of mixtures of barium acetate and formate, Bell & Reed (8) observed a small decrease in the  $\text{C}^{13}$  content of the carbonyl carbon in the acetaldehyde product relative to that of the original salts.

The authors believe that this difference may be attributable to combustion error (53). A similar conclusion is the result of a study by Arnstein (56) on the combustion of choline  $C^{14}$ -labeled in the methyl groups.

Eischens (57) has published the results of an investigation of the exchange between gaseous CO and CO chemisorbed on iron; the exchange data show the iron surface to be heterogeneous. Within the experimental precision of about 1 per cent there was no difference in the rates of exchange of  $C^{13}O$  and  $C^{14}O$ .

Two papers have appeared on the abundance of the carbon isotopes in natural carbon sources. Von Eckermann, von Ubisch & Wickman (58) measured the isotopic composition of carbon from some alkaline intrusions. No particular regularities were noticed among these carbonate rock analyses. Wickman (59) reported the results of a broad survey of the relative abundances of the carbon isotopes in plants. A total of 105 plants representing all the major systematic groups were subjected to analysis. There were no systematic differences between the groups except perhaps for gymnosperms. There were, however, large differences in carbon isotope content between plants grown in different biotopes (areas of uniform environmental condition), and these differences are related to the varying intensity of the local  $CO_2$  cycle. For example, the largest isotope effect in  $CO_2$  uptake is found in tropical rainforest trees where the conditions of growth are such that the local atmosphere is very stable with respect to  $CO_2$  and where soil respiration is favored; the smallest effects are found for plants grown in windy places where the local atmosphere has little chance to develop and soil respiration is negligible. These observations are exactly the reverse of what one would predict upon the assumption that  $CO_2$  uptake is a one-step rate process.

Bigeleisen (60) has reviewed the general theory of the effect of isotopic substitution on the rates of chemical reactions, and has considered from a theoretical standpoint the results of a large number of published investigations. The following intramolecular isotope effects are treated briefly: decarboxylations of malonic acid (31, 33, 34, 35, 61), bromomalonic acid (35), and oxalic acid (46, 47). Among the intermolecular isotope effects discussed are: decarboxylation of malonic acid (31,32), alkaline decomposition of trichloroacetate ion (62), decarboxylation of mesitoic acid (40, 41), hydrolysis of ethyl benzoate (63), Cannizzaro reaction on benzaldehyde (64), benzoin condensation (64), and benzoic acid rearrangement (64).

In most cases, consideration of the mechanism of the reaction permits agreement to be achieved between the theoretical calculations and the experimental results. The calculation for the ethyl benzoate hydrolysis is in error; the model adopted for malonic acid decarboxylation yields predictions at variance with experiment on the  $C^{14}$  effect; the prediction of this model for  $(k_4/k_3 - 1)$  in the decarboxylation of malonic acid-1- $C^{13}$  does not depend upon any molecular parameters and yet is 25 per cent lower than the experi-

mental finding in the most complete study (33); the predicted value of  $(k_{12}/k_{14} - 1)$  for the decarboxylation of carboxyl-labeled mesitoic acid is 25 per cent lower than that observed. In all the cases just listed the application of the theory appears to yield unsatisfactory results. However, in view of the other successes of the theory it may well be that it is the experiments on these rather complicated systems which are at fault, at least in some cases.

Eyring & Cagle (25) have treated briefly the isotope effects in the dehydration of  $\text{HCOOH}$  (65) and oxidation of carboxyl-labeled  $\text{CH}_3\text{COOH}$  (53), and show graphs of the temperature dependence of the separation factors for the rupture of  $\text{C}^{12}\text{-C}^{12}$  versus  $\text{C}^{12}\text{-C}^{14}$  and  $\text{C}^{12}\text{-O}^{16}$  versus  $\text{C}^{14}\text{-O}^{16}$ . In the printed discussion of this paper Bernstein and Bigeleisen criticize the experimental value for the temperature coefficient of the  $\text{HCOOH}$  dehydration isotope effect (65).

#### ISOTOPES OF NITROGEN

A summary of experiments on nitrogen isotope effects to late Autumn 1952 is given by Ropp (26).

Stacey, Lindsay & Bourns (66) have determined several isotope effects in the thermal deamination of phthalamide. With  $\text{N}^{14}\text{H}_3$  instead of  $\text{C}^{12}\text{O}_2$  and  $\text{N}^{15}\text{H}_3$  instead of  $\text{C}^{13}\text{O}_2$ , etc., the notation used in the discussion of malonic acid decarboxylation will be employed here. At  $180^\circ\text{C}$ .  $k_4/k_3 = 1.014 \pm 0.002$ . At  $180^\circ$ ,  $190^\circ$  and  $210^\circ\text{C}$ ., respectively,  $k_1/2k_3 = 1.006 \pm 0.001$ ,  $1.006$  and  $1.008$ , while  $k_1/2k_4 = 0.994 \pm 0.001$ ,  $0.994$  and  $0.996$ . In a theoretical evaluation of these results, Bigeleisen (67) shows that they are in agreement with the predictions of theory and gives an interesting proof that the reduced mass effect is the same whether isotopic bonds are being formed or ruptured. In the case at hand,  $k_1/2k_4$  is less than unity because the contribution of the activated complex frequencies to the free energy factor in the rate constant ratio is larger than that of the normal molecules and has negative sign. Bigeleisen also demonstrates that the rate determining step in the deamination cannot be a cyclization involving simultaneous rupture and formation of  $\text{C-N}$  bonds.

The data of Clusius and Hurzeler (68) apparently imply an appreciable isotope effect in the oxidation of  $\text{NO}_2^-$  to  $\text{NO}_3^-$ .

#### ISOTOPES OF OXYGEN

Dole (69) has written a detailed review of the chemistry of the oxygen isotopes; the summaries are complete up to March 1952 and are accompanied by complete discussions of some of the more recent work. Among the topics reviewed are: measurement and separation of the isotopes of oxygen; their exchange in inorganic salt solutions, between the gas and solid oxides, and between organic compounds and water; the use of oxygen isotopes in the study of the mechanisms of organic and inorganic reactions; variations in the natural abundance of the oxygen isotopes and the atomic weight of oxy-

gen. Studies on the effect of oxygen isotope substitution on the rates of chemical reactions are also summarized in Ropp's review (26). Bigeleisen (60) gives brief mention to the isotope effects in the decomposition of  $\text{NH}_4\text{NO}_3$  (70).

Rutenberg & Taube (71) have measured rates and equilibria in the exchange of solvent water with the aquopentammine cobaltic ion. The equilibrium constant for the reaction  $\text{Co}(\text{NH}_3)_5\text{H}_2\text{O}^{16+3+} + \text{H}_2\text{O}^{18} = \text{Co}(\text{NH}_3)_5\text{H}_2\text{O}^{18+3+} + \text{H}_2\text{O}^{16}$  was found to be  $1.019 \pm 0.001$  at  $25^\circ\text{C}$ . This is a somewhat smaller effect than that found in the corresponding equilibrium involving the ion  $\text{Cr}(\text{H}_2\text{O})_6^{3+}$  (72).

Feder & Taube (73) have reported extensive results on isotope fractionation incident to ionic hydration. Enrichment factors as functions of solute concentration were obtained for  $\text{Mg}(\text{ClO}_4)_2$ ,  $\text{HCl}$ ,  $\text{LiCl}$ ,  $\text{NaI}$ ,  $\text{AgClO}_4$ , and  $\text{NaClO}_4$ . Single experiments were performed on  $\text{Co}(\text{en})_3\text{Cl}_3$ ,  $\text{Cr}(\text{ClO}_4)_3$ ,  $\text{MgCl}_2$  and  $\text{Mg}(\text{ClO}_4)_2$ . All of the enrichment factors are less than 1 per cent and required the use of a high precision mass spectrometer for their estimation.

Cahill & Taube (74) have determined the relative rates of reaction of  $\text{H}_2\text{O}_2^{16}$  and  $\text{H}_2\text{O}^{16}\text{O}^{18}$  in a number of oxidations, reductions, and catalytic decompositions. Typical values of  $k_{16}/k_{18}$  (near  $25^\circ\text{C}$ . unless otherwise specified) for various reactions and agents are as follows: reductions— $\text{Fe}(\text{II})$  1.071,  $\text{Sn}(\text{II})$  1.060,  $\text{Ti}(\text{III})$  1.003 ( $4^\circ\text{C}$ .),  $\text{Cr}(\text{II})$  0.97,  $\text{Cu}(\text{I})$  0.95; oxidations— $\text{Ce}(\text{IV})$  1.011,  $\text{Cl}_2$  1.010,  $\text{HOCl}$  1.008; catalytic decompositions— $\text{Fe}(\text{III})$  1.007. The results are employed in elucidations of the various reaction mechanisms involved.

Dole *et al.* (75) investigated the fractionation of oxygen isotopes in the catalytic decomposition of  $\text{H}_2\text{O}_2$  by  $\text{MnO}_2$ ,  $\text{FeO}_3$ , colloidal  $\text{Au}$ ,  $\text{Pt}$ , and soluble catalase. Except for catalase the fractionation is about 1.5 per cent. Catalase produces no net fractionation, but impoverishment and enrichment are observed during the decomposition.

Hunt & Taube (76) determined fractionation effects in the photochemical decomposition of  $\text{H}_2\text{O}_2$ . Data are tabulated for the fractionation for the production of oxygen, water, and products irrespective of their identity, but do not lend themselves to summary here.

#### ISOTOPES OF SULFUR

Macnamara *et al.* (77) measured the  $\text{S}^{32}/\text{S}^{34}$  ratio of sulfur obtained from a variety of sources. The near identity of ratio for igneous rock sulfur and that from meteoritic troilite is taken as evidence for their common origin. In general, sulfates and sulfides ore are enriched in  $\text{S}^{34}$  while organic sulfur and sedimentary sulfur are impoverished. Some of these relations can be understood in terms of the earlier work of Thode, Kleerekoper & McElcheran (78) which demonstrated that  $\text{H}_2\text{S}$  formed from sulfate by the reducing bacteria *Vibrio desulfuricans* is depleted in  $\text{S}^{34}$  by about 1 per cent.

## ISOTOPES OF MERCURY

McDonald & Gunning (79) saturated dry air with Hg vapor at 25°C. The vapor flowed down a long tube which was irradiated near the downstream end with a  $\text{Hg}^{198}$  discharge tube; the total gas pressure was about 8 mm. The Hg in the  $\text{HgO}$  which was deposited upstream from the irradiated end was subjected to isotope analysis. The following are the approximate atom percentages of the various isotopes in natural Hg and that obtained from the  $\text{HgO}$ : 196 (0.15 natural, 0.01 deposited), 198 (10.1, 0.16), 199 (17.0, 10.7), 200 (23.3, 18.2), 201 (13.2, 24.6), 202 (29.6, 14.3), 204 (6.7, 32.0). The reduction in 198 percentage is attributable to self reversal in the source which was run hot at 150° C. That the reversed emission line is quite broad is shown by the enrichments of masses 201 and 204.



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# RADIATION DOSIMETRY AND PROTECTION<sup>1</sup>

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## INTRODUCTION

The Recommendations (1) of the International Commission on Radiological Units (London, 1950) have marked, in a sense, the official coming of age of radiation dosimetry. By international agreement the term "radiation dose" has assumed for the first time the unambiguous meaning of increment of energy per unit mass in the irradiated object and not merely the result of a particular type of ionization measurement of the incident radiation.

The official unit of dose is the erg/gm. The unit previously used, the roentgen, has been retained for photon radiation below 3 Mev by virtue of its wide acceptance in Radiology and in recognition also of the fact that below this limit, exposure in roentgens is related to the energy absorption in most biological tissues by a sensibly constant factor of proportionality.<sup>2</sup>

The reasons for the abandonment of the roentgen as a universal unit of dose have been treated at length in the literature (4, 5, 6) and they will not be discussed here. It will suffice to comment that, by virtue of the new unit adopted, the concept of dose remains unaltered whatever the type and energy of the ionizing radiation, and that, in principle at least, the measurement of radiation dose need not necessarily involve a measurement of ionization.

In most instances, however, measurements of gas ionization in cavity chambers are likely to remain the method of choice for some time because of their relative ease and because of the basic property of the chamber which is represented by the familiar expression of Gray (7).

$$D_m = J_m W \rho_m \quad 1.$$

In this equation,  $D_m$  is the dose in the walls of the cavity in ergs/gm.,  $J_m$  is the number of ion pairs per unit mass of gas in the cavity,  $W$  the energy in ergs necessary to form a pair of ions in the gas, and  $\rho_m$  the ratio of the mass stopping power of the wall material to that of the gas for the ionizing particles associated with the incident radiation. Some readers will recall that accept-

<sup>1</sup> The survey of the literature pertaining to this review was completed in March, 1953.

<sup>2</sup> Where conditions of photon equilibrium are attained and photon scattering is avoided, the exposure to one roentgen of  $\gamma$ -radiation results in the transfer of 93 ergs to each gram of soft tissue over a wide range of photon energies (2, 3). The wide adoption of the rep as a unit of dose is based on this fact and on the desire of expressing energy absorbed in numbers essentially identical to the corresponding exposure expressed in roentgens.

ance of equation 1 in the late thirties followed the demonstration of its ability to: (a) Predict the relative ionization in chambers composed of walls of different  $Z$  exposed to the radium gamma radiation (8); (b) Measure the gamma ray energy emission from radium and thorium in fair agreement with calorimetric measurements (8); (c) Yield dose rates in roentgens from filtered radium and thorium sources consistent with the gamma ray spectra of these elements and with the known laws of photon absorption in light elements (9) and in agreement with measurements made by the standard open air chamber (10, 11).

To be sure, the agreement was not of very high order in all cases but, in view of the heterochromaticity of the sources then available, and the uncertainty in the values of  $W$  and  $\rho$ , not much more could be expected.

In what follows your reviewer will comment mostly on recent evidence related to the usefulness of equation 1 in the dose measurement of photon and neutron radiation of widely different energies with special emphasis on comparisons with calorimetric measurements when available, and with some discussions on the most recently determined values of  $\rho$  and  $W$ . Lack of adequate space prevents review of dosimetric techniques employing photographic emulsions, scintillation techniques, or chemical effects. The sketchy comments on their status which have been published elsewhere (12, 13) must be considered partly obsolete at this time.

#### MEASUREMENT OF PHOTON RADIATION

For the specific case of photon radiation, this review will be subdivided under headings arbitrarily called Grenz Rays, Medium Soft X-Rays, Hard X-Rays, and Photons above 3 Mev. This subdivision reflects only in part the range of facilities available for photon production; it follows instead, more closely the predominant factors influencing the measurement of dose by means of equation 1 and the methods hitherto employed to test its correctness.

*Grenz rays.*—In this region the dose is customarily expressed in roentgens and most easily measured with a standard open air chamber (14, 15).

Despite several attempts, the use of cavity ionization chambers has not come into wide use principally because the wall thickness required to limit absorption of the primary beam is incompatible with ordinary ruggedness. Tests on a commercially developed chamber have been reported (16, 17) and have shown the necessity of adopting caution in interpolating or extrapolating the calibration constants of the chamber within this soft region. It has been proven, however, that it is possible to construct special ionization chambers which maintain their calibration within a limited range of qualities (18).

For the purpose of measuring tissue doses, extrapolation chambers have been used. Here the main difficulty consists in evaluating the wall effect since, due to the small penetration of the secondary electrons and the predominance of the photoelectric effect, the conductive coating and the linear

dimensions of the air space play a predominant role in the interpretation of the ionization measurements (18, 19).

Attributable, probably, to the ease with which ionization measurements with small open air chambers are possible, no effort at accurate correlation between ionization and calorimetric measurements has been made in this region. However, sufficiently high fluxes are available from x-ray tubes supplied with beryllium windows (20).

*Medium soft x-rays.*—From energies of about 0.025 to a few Mev the cavity ionization chamber is the most widely used instrument for the measurement of dose. Its constants are determined by comparison with the standard open air chamber until photons of about 0.4 Mev are reached. Beyond this limit, the dimensions of the latter become cumbersome and the use of thimble chambers is predicated either upon the validity of formula 1, or on calibration at lower energies. The value of  $W=32.5$  ev for air is generally adopted and the values of  $\rho$  calculated either by Laurence (21) or by Gray (7) are deemed sufficiently accurate for the purpose although, strictly speaking, these values apply only when no photoelectric absorption takes place in the walls of the chamber and secondary electron energies come within the scope of the Bethe-Bloch theory.

In order to minimize the photoelectric correction and to compensate for photon absorption in the walls, there has been a tendency to include in walls made largely of organic compounds, small amounts of some element of relatively high atomic number. Some of the pitfalls in this practice have been demonstrated by Wilson and co-workers (22, 23, 24) who set out to test the validity of equation 1 for relatively high  $Z$  and low photon energy. Under these conditions the equivalent of expression 1 has been customarily written as:

$$D_m = J_m W \rho_m = n_{hp} E (\sigma_a + \tau_z) n_0 \quad 2.$$

where

$\sigma_a$  = Compton absorption coefficient per electron in  $\text{cm}^{-2}$

$\tau_z$  = photoelectric absorption coefficient per electron in wall of atomic number  $Z$  in the same units

$n_{hp}$  = number of incident photons per  $\text{cm}^2$

$E$  = energy of photon

$n_0$  = number of electrons per unit mass of wall material.

Although their estimate of  $E$  from heterogenous x-rays is open to criticism, their results show conclusively that the ionization does not follow equation 2 but approximates an equivalent one in which the photoelectric conversion  $\tau_z$  is replaced by  $\tau_z(E - E_k)/E_k$ , where  $E_k$  is the binding energy of the  $K$  shell. It seems obvious that lack of monochromaticity precluded attainment of accuracy high enough to assess the importance of the fluorescent yield  $f$ , for the photoelectric conversion should more properly be expressed by

$$\tau_z(E - fE_k)/E, \quad f < 1.$$

On the basis of their findings it seems wise, therefore, to incorporate in the chamber walls elements with  $Z$  as close as possible to that of air, if a "K jump" effect is to be avoided.<sup>3</sup>

A question may be raised at this point. If experimental conditions are favorable for the accurate computation of the energy absorbed in a thin wall, it should be possible to determine experimentally the values of the product  $W\rho$  in the energy regions where the velocity of the ionizing electrons is lower than the velocity of the electrons in the various shells of the atoms of the wall, and hence to obtain, rather easily, information as to the values of  $dE/dx$  in a region where theory is not very helpful. Monochromatic sources should not be too difficult to obtain, since good intensities can be had by the method of fluorescent radiation (25, 26) or by the use of suitable radioelements. It will be conceded that the method is not as direct as some others used in the investigations of  $dE/dx$  but it should still be capable of setting some limits on the deviations to be expected from theory.

*Hard x-rays (0.3–3 Mev).*—This region, characterized by the virtual abandonment of the standard air chamber as the basis of comparison, has been used extensively in recent investigations of the properties of the thimble chamber. The character of the tests performed, however, has not changed radically from those previously mentioned.

Although the task should have been lightened by the availability of radioelements emitting monochromatic radiation, there has been as yet no reported experimental verification of the computed relationship (27) between  $r/hr.$  at 1 cm. and mc. content of gamma ray sources. This should not be altogether unexpected, however, because methods for the accurate standardization of radioelements have been reported only recently (28, 29, 30).

Comparison between standard air chamber, extrapolation, and thimble chamber measurements have been published by Grove (31) who used sources of  $Cs^{137}$  (.661 Mev) and  $Co^{60}$  (1.17 and 1.33 Mev). The agreement, as stated by the author, is within 2 per cent for the case of  $Cs^{137}$  and better than 1 per cent for the case of  $Co^{60}$ . Unfortunately, these limits do not indicate to what extent formula 1 is verified, because the thimble chamber was calibrated with radium gamma rays and the extrapolation chamber reading was not corrected for the stopping power ratio  $\rho_m$  of the wall material (lucite) to air. However, a hurried correction performed by your reviewer, based on Laurence's calculation, yields agreement within the author's own estimate of over-all experimental error ( $\pm 2$  per cent).

Within this energy range direct comparison between calorimetric and ionization measurements have been reported in abstract form by Laughlin, Beattie & Ovadia (32). The forthcoming manuscript (33) has been made

<sup>3</sup> The use of fluorocarbons is to be recommended on theoretical grounds. The use of analogous gaseous compounds would offer the added advantage of high gas density. These possibilities are under investigation by the writer at the Argonne National Laboratory.



available in advance to your reviewer through courtesy of the authors. The flux density originating from an x-ray tube operated at 400 kv and filtered by 1.75 mm. of copper, was determined calorimetrically, and found to be  $2880 \pm 90$  ergs/sq. cm. per r, the latter as measured by a Victoreen chamber calibrated by the manufacturer. This value is in good agreement with the value of 3000 erg/sq. cm. per r calculated, assuming a Kulenkampff x-ray spectrum from the tube duly corrected for attenuation in the filter. Of definite interest is the author's determination of the flux density by means of integration of the ionization measurements in depth of copper-lead and lead phantoms which yielded figures of 3400 and 2500 erg/sq. cm. per r respectively, when the relative stopping power of these materials to air are calculated by the Bethe-Bloch formula. No attempt was made to explain this discrepancy although it undoubtedly merits further investigation; in view of the excellent consistency that this method gives at much higher energies (*vide infra*) one is inclined to surmise that, barring some experimental *faux-pas*, these results may be an indication of either a failure of the theoretical stopping power law for these electron energies and materials, or omission of the "jump" effect at the K absorption limits (*vide supra*).

Before proceeding further, it should be noticed that the photon energy region 350 to 750 kev is unusually favorable for the comparison just mentioned since the value of the flux per roentgen in this region is not critically dependent on photon energy and ionization measurements are still possible with standard air chambers operated at moderate pressures. It is to be hoped that the availability of  $\text{Cs}^{137}$  (661 kev) as a photon source of high specific strength will eventually stimulate similar attempts of higher precision.

An excellent technique for the study of the Bragg-Gray relationship consists in incorporating  $\beta$ -ray-emitting isotopes in the walls of the cavity ionization chamber and correlating the ionization therein to the concentration of the isotopes in the walls. The relationship is obviously:

$$n_{\beta} \bar{E}_{\beta} = J_m W \rho_m \quad 3.$$

where  $n_{\beta}$  is the number of beta particles (emitted per unit mass in the walls) which produces  $J_m$  ions per unit mass of gas in the cavity, and  $\bar{E}_{\beta}$  is the average beta ray energy per disintegration. The actual prospects of utilization of this method are predicated on the relative accuracy with which the various factors in equation 3 are known. In view of the progress made in the determination of  $n_{\beta}$  and the claims of accuracy on the values of  $\bar{E}_{\beta}$ , one would expect that these prospects are excellent; for instance, the wide range of beta energies available should provide a good opportunity to determine the values of  $W\rho_m$  with relative economy of instrumentation.

Several papers have appeared dealing directly or indirectly with this subject (34 to 38). Caswell (38) used an extrapolation chamber with aqueous electrodes and took  $W=32.5$  ev for air, and  $dE/dx$  as calculated by Wang (39) for air on the stopping power theory of Bethe with corrections by Halpern & Hall (40). He reports agreement of 1.0, 0.6, 6.0, and 0.5 per cent with

the values of  $\bar{E}_\beta$  reported in the literature for  $P^{32}$ ,  $Y^{90}$ ,  $I^{131}$ , and  $Ca^{45}$ , respectively. The magnitude of the discrepancy with  $I^{131}$  is not entirely unexpected since the decay scheme of Metzger & Deutsch (41), assumed by the author, has been found to be not entirely correct in subsequent work and it is indeed, still the object of intensive scrutiny (42). The results on  $P^{32}$  seem to be of particular importance, in view of the excellent interchecks existing on absolute disintegration rates, calorimetric determination, and spectral composition of the emitted particles. However, Baily (37), evaluating  $dE/dx$  by means of equation 3, finds disagreement with the theory of stopping power of Bethe when both  $P^{32}$  and  $S^{35}$  are used in extrapolation chambers with walls containing these elements as compounds of potassium and lead.

*Photons above 3 Mev.*—This region is characterized by the interaction of the photon with the nucleus (pair production, nuclear disintegration) and by the fact that the mean free path of the secondary electrons becomes comparable to the mean free path of the primary photons. In the presence of these phenomena, the roentgen ultimately loses much of its significance and usefulness as a unit of dose and, consequently, the use of the parallel plate chamber as a standard instrument is altogether pointless.

Investigations in this region have been concerned with the use of the cavity chamber for the measurement of flux and with the assessment of its basic properties by comparison with calorimetric measurements.

For the latter we are indebted mainly to Laughlin and co-workers. In the first experiments reported (43) the energy flux of a collimated beam (2.4 cm. diameter) from a betatron operated at 22.5 Mev was measured by the heat increase produced in a lead cylinder 3 cm. thick and 4.2 cm. in diameter. The percentage of the flux absorbed in the lead block was calculated from a "depth dose" curve obtained with a shallow ionization chamber (1 mm. thick) and with photographic emulsions placed at different depths in a similar lead block. The distribution of the energy absorbed in the depth was assumed to be the same as the distribution of ionization, and the film blackening gave no evidence of energy escaping through the sides of the lead block. Measurements with a thimble chamber surrounded by an 8 cm. cube of water were also made under the same conditions. The result was  $4580 \pm 95$  ergs/sq. cm. per e.s.u./cc. in the chamber. If corrections suggested by Mayneord (44) for the interpretation of the  $r$  at these energies are applied, the flux per  $r$  becomes 4630 ergs/sq. cm. which is the theoretical value expected from a monoergic beam of 5 Mev photons. Because of the heterochromaticity of the photon beam, no critical evaluation of Gray's equation could be made at that time. However, in a later publication (45) Laughlin compares the calorimetrically determined energy flux with the energy absorbed per sq. cm. by an "infinitely" thick water phantom throughout the depth of which the energy absorbed was studied with a thimble ionization chamber. By integration of the latter, he obtained a value of 98 ergs per gram-roentgen—as compared with a calculated value of 90.7. In view of the many experimental difficulties this agreement must be considered good. Laughlin offers the

opinion that the greatest experimental error lies in his determination of the gram-roentgens from his incomplete depth-dose curve in water. The writer would suggest also that side losses from the beam should be investigated more thoroughly and that the calculation of the fraction of the beam absorbed in the calorimeter block by "depth dose" curves in Pb needs closer scrutiny; on the basis of the wide range of energies possessed by the secondary electrons as the beam reaches greater depths, proportionality between ionization in air and energy absorption may not be entirely justified in view of the great disparity in atomic numbers involved. This objection would disappear if, instead of approximately 75 per cent, more than 95 per cent of the energy of the beam were absorbed in the calorimeter block.<sup>4</sup>

At higher energies, direct comparison between calorimetric and ionization measurements relevant to this discussion have not been reported, but the use of the ionization chamber as a method of measuring energy flux from accelerators and nuclear reactions has been rather extensive and consequently a variety of calculations on ionization chamber sensitivities have appeared (46, 47, 48).<sup>5</sup> For the purposes of our review, the more detailed calculations of Fowler *et al.* (47) are of greatest interest inasmuch as these authors have evaluated the contribution to ionization of the secondary Compton photons released in thick walls and have verified experimentally its essential correctness at thickness greater than the thickness of maximum ionization.

At energies of 330 Mev, Blocker *et al.* (49) have evaluated the flux in betatron x-ray beams by "depth dose" curves in large blocks of lead, copper, aluminum, and carbon using flat ionization chambers with very thin aluminum walls. By integration of the areas under these curves and by use of equation 1, excellent consistency was obtained as to the value of the flux. The conversion of energy in the various materials was evaluated in terms of the theory of bremsstrahlung and of Lawson's (50) values for pair production. The value of  $\rho$  used was calculated from the theory of electronic stopping power near minimum ionization (51).

It is rather unfortunate that the reported calorimetric measurements (52, 53, 54) in this region have not been correlated with ionization measure-

<sup>4</sup> In a forthcoming publication (33) kindly made available in manuscript by the authors, detailed results from a similar experiment are presented. The calorimeter block was extended from 3.0 to 13 cm. and beams of two different diameters were used. Energy fluxes of  $5700 \pm 250$  and  $5350 \pm 250$  ergs/sq.cm./r were obtained, respectively, where calorimetric measurements and integration of the "depth dose" curve in water were compared. The theoretical flux per r, based on the existence of a Schiff photon spectrum and on Mayneord's calculations for monoergic photons, was 5200-5400 erg/sq.cm./r.

<sup>5</sup> It should be noted that in these calculations the values of  $\rho = dE/dx$  (medium) /  $dE/dx$  (gas) are perforce the ratio of total stopping power in the wall to collision stopping power in the gas, since the object is to measure the total energy of the incident beam. In analogous calculations of energy utilization in an irradiated medium,  $\rho$  must be assessed in terms of energy losses due to collisions only, since the only relevant entity under consideration is the flow of electrons through the gas cavity.

TABLE I  
ENERGY W(eV) SPENT PER ION PAIR FORMED BY IONIZING PARTICLES IN VARIOUS GASES

Particle	Authority and Method*	A	He	H <sub>2</sub>	N <sub>2</sub>	Air	O <sub>2</sub>	CH <sub>4</sub>	CO <sub>2</sub>	C <sub>2</sub> H <sub>6</sub>	C <sub>4</sub> H <sub>10</sub>	C <sub>2</sub> H <sub>2</sub>	C <sub>2</sub> H <sub>4</sub>
Po $\alpha$	(90, 91, 139) Jesse I.C.	26.4	42.7	36.3	—	—	—	29.2	34.5	26.6	—	27.5	28.0
Pu $\alpha$	(137) Sharpe I.C.	26.3	—	—	36.4	35.6	32.9	29.1	34.2	—	—	—	—
Pu $\alpha$	(138) Bortner, <i>et al.</i> I.C.	26.2	~42.0	—	36.3	—	—	29.6	—	—	25.9	—	28.0
Po $\alpha$	(56) Valentine, <i>et al.</i> P.C.	25.9	31.7	37.0	36.0	35.2	32.2	29.0	—	—	—	—	—
Absolute Values for $\alpha$ Particles													
Relative Values for $\alpha$ Particles													
U $\alpha$	Av. Values from above (93)	.74	1.20	1.03	1.02	1.00	.92	.82	.97	.75	.73	.78	.79
Po $\alpha$	Rossi I.C. (75)	—	—	—	1.05	1.00	.93	.83	.97	—	—	.78	.80
	Bretscher & French I.C.	—	—	—	—	1.00	—	—	—	—	—	.79	.81
Absolute Values for Electrons and Protons													
A <sup>37</sup> & H <sup>3</sup> Electrons	(56) Valentine, <i>et al.</i> P.C.	27.0	32.5	38.0	35.8	35.0	32.2	30.2	—	—	—	—	—
H <sup>+</sup> (340 Mev)	(98) Bakker, <i>et al.</i> I.C.	25.5	29.9	35.3	33.6	33.3	31.5	—	—	—	—	—	—

\* I.C.—Ionization Chamber.  
P.C.—Proportional Counter.

ments of the type just described, for the need is indeed acute and the role of photonuclear reactions in radiological safety is yet to be explored.

Interested readers will find a thorough discussion of the various aspects of photon dosimetry above 3 Mev, complete with bibliography, in a forthcoming publication of the National Committee on Radiation Protection (55).

*Status of  $W$  and  $\rho$  for electrons.*—Not many reports have appeared on the value of  $W$  for electrons in gases likely to be used in radiation dosimetry. Several of these have originated from the University of Glasgow where proportional counters containing  $A^{37}$  and  $H^3$  have been used. In their latest publication, Valentine & Curran (56) present what they consider the most reliable values for a number of gases. (See Table I.) Of concern to radiological physicists is a previous statement (57) questioning the validity of Gerbes' (58) equation which has generally been assumed valid in the energy range 0.3 to 60 kev. In view of the impurity of the gas used (0.7 per cent methane) and the experimental error ( $\pm 2$  per cent) these results cannot be considered significantly at variance with Gerbes' formula. There are, however, experimental indications that above 48 kev,  $W$  does not vary to any great extent, for Bailly (37) reports  $\bar{W} = 32.5$  ev for  $S^{35}$   $\beta$ -rays ( $\bar{E}_\beta = 48.1$  kev), Clark & Brar (59) indicate  $\bar{W} = 32.5$  ev for  $P^{32}$   $\beta$ -rays ( $\bar{E}_\beta = 700$  kev), and Laughlin *et al.* (60) obtain  $W = 33$  ev for 17 Mev electrons.

Our concepts as to the values of  $\rho_m$  in the Bragg-Gray equation must be revised somewhat in the light of the polarization effect in condensed systems for particles of high energy (61). Inasmuch as the extranuclear interactions of electrons and  $\gamma$ -radiation are being reviewed elsewhere in this volume, this effect will not be discussed here.

For the benefit of the reader, however, the writer has obtained from

TABLE II  
STOPPING POWER PER ELECTRON RELATIVE TO AIR FOR FAST  
BETA PARTICLES OF ENERGY  $E^*$

$E(\text{Mev})$	Be	$(CH_2)_n$	C	Poly- styrene	Lucite	Mg	Al
0.5	1.036	1.051	1.007	1.038	1.031	0.950	0.946
0.75	1.023	1.038	1.000	1.030	1.022	0.952	0.950
1.0	1.012	1.028	0.992	1.020	1.014	0.951	0.949
1.5	0.997	1.009	0.977	1.003	0.997	0.947	0.944
2.0	0.985	0.995	0.963	0.988	0.982	0.942	0.936
3	0.968	0.976	0.944	0.969	0.963	0.932	0.926
5	0.937	0.948	0.919	0.942	0.937	0.911	0.903
10	0.897	0.911	0.884	0.907	0.901	0.879	0.866
20	0.856	0.879	0.848	0.870	0.865	0.850	0.835
50	0.816	0.830	0.804	0.826	0.821	0.811	0.799
100	0.802	0.815	0.791	0.813	0.808	0.799	0.789

\* From Sternheimer (62).

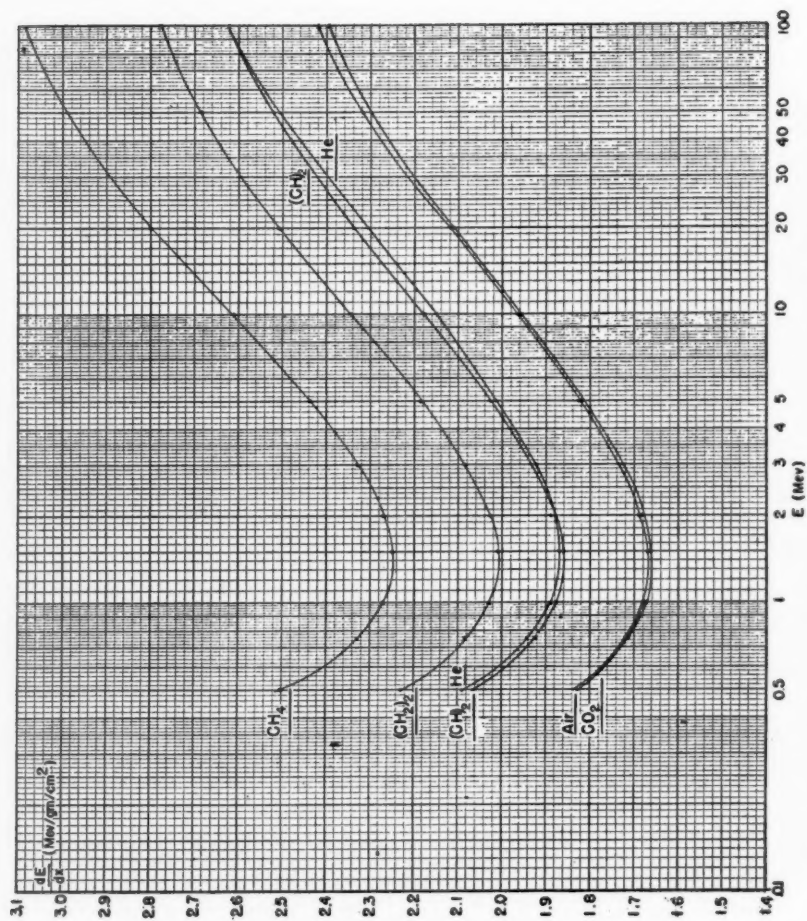


Fig. 1. Stopping powers for electrons in various gases. [R. M. Sternheimer (62)].



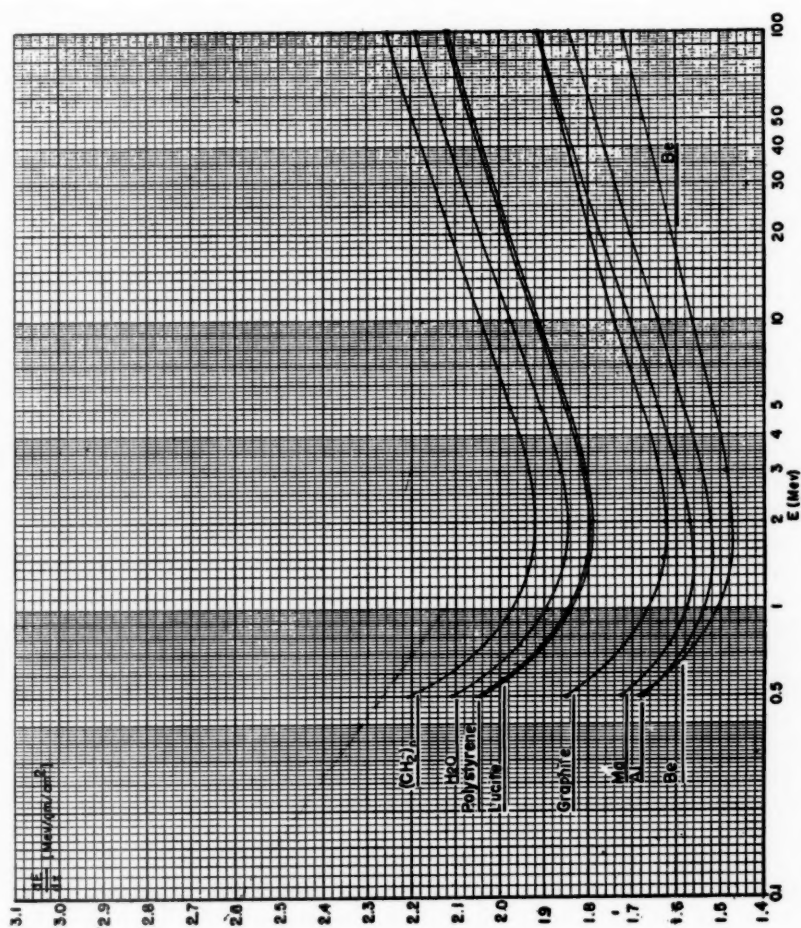


FIG. 2. Stopping powers for electrons in various solids [R. M. Sternheimer (62)].

R. M. Sternheimer considerable theoretical data on the average rate of energy loss of electrons in several solid and gaseous materials of interest in radiation dosimetry. These calculations, based on methods already published (62), are shown by permission of their author in Figures 1 and 2 and in Table II.

Before closing this subject it may be well to recall that in photon dosimetry the proper values of  $\rho_m$  and  $W$  are not strictly those corresponding to the average energy of the secondary electrons. More accurate expressions have been published by Laurence (21), Fowler *et al.* (46), and Wang (39) on the basis of the initial electron spectrum released. Laughlin *et al.* (60) have computed average values of  $\bar{p}$  (water versus air) for monoergic electrons of high energy on the basis of the  $\delta$ -ray spectrum engendered by electronic collisions.

Finally, welcomed, I am sure, by the harassed hospital physicist, Johns and co-workers (63, 64) have published extensive tables on the initial distribution of electrons released by photons of therapeutic interest and have calculated also the corresponding specific ionizations.

#### NEUTRON DOSIMETRY

*Ionization methods.*—Two excellent reviews have appeared recently on the subject of measurement of neutron flux and neutron energy distribution (65, 66). Although in principle the neutron dose can be computed roughly from these parameters by means of well-known expressions (67), the computational approach remains of very limited usefulness in practice (68), and definitely hopeless in personnel-monitoring work. Basic neutron dosimetry, therefore, has been oriented toward the development of usable cavity ionization chambers for which the fundamental relationship of Gray can be considered valid. Owing to the difficulties of using a gas volume of linear dimensions small compared to the range of recoil nuclei, use must be made of chambers in which walls and gas filling are composed of chemical elements identical (both in nature and in proportion) to those of the irradiated biological system.

Rossi & Failla (68) have simulated the composition of typical tissue ( $C_8H_{40}O_{18}N$ ) by means of a special gel and special plastic lining of suitable electric conductivity and have reported close agreement between the two when the chambers were exposed to neutrons in the energy range 0.5 to 14 Mev (69). These authors report some difficulties with the stability of the tissue equivalent gas mixture and suspect adsorption by the plastic wall. This reviewer, using identical plastic lining and filling, but different structural materials, has obtained with known Po-B and Po-Be sources preliminary results consistent with theoretical predictions based on both neutron (70, 71) and  $\gamma$ -ray spectra of these sources (72, 73, 74). This chamber retained its calibration for a period of five months, at which time it was accidentally broken. It seems apparent therefore that, except for some uncertainty in the values of  $W$  and  $\rho$  (*vide supra et infra*), designs of suitable "tissue" ionization chambers are at hand for reliable measurement of total dose of mixed radiations.

In radiobiological and health physics laboratories, however, irradiation by neutrons is generally accompanied by gamma radiation. Since the biological effect of neutrons, is, per equal dose, considerably greater than that of photons, it is important to know the energy imparted by each component, and for this purpose the tissue chamber *per se* is of no avail.

Several methods aimed at the solution of this problem have been proposed. The "twin" ionization chamber method, originated by Bretscher & French (75, 76), is based on the use of two chambers which respond equally to photons but not to neutrons. Balance with photons is accomplished by adjustment of gas pressure, and different neutron sensitivity is achieved by variation in hydrogen content. To estimate dose, "homogenous" chambers are required, namely, chambers having gas and walls of identical molecular composition such as (a) ethylene-polythene, (b) acetylene-polystyrene, and (c) deuterioethylene-deuteropolythene. From the standpoint of accuracy the combination (a)(c) is preferable since  $\bar{W}$  and  $\rho$  should remain constant for all conditions of photon irradiation. These authors have calculated theoretically the ratio of the difference  $J_1 - J_2$  of the ionization in the two chambers to the ionization  $J_1$  in chamber (a) and verified it experimentally by the use of pure neutron beams of known energy. They have also shown that the fraction of the ionization current in chamber (a) due to the neutron component of a mixed beam is given simply by the ratio of  $(J_1' - J_2')/J_1'$ , obtained in the mixed beam, to the value  $(J_1 - J_2)/J_1$  obtained with a pure neutron beam of the same energy. When dealing with neutron beams of known energies, the use of the deuterated compounds yields results as accurate as others devised for the purposes of standardization (77) and it is amenable to greater accuracy as the knowledge of  $\bar{W}$ ,  $\bar{\rho}$  and neutron-deuteron interaction is improved. The "twin" chamber combination (a)(b) has been used recently by Dainty (72) in his measurements of dose rates in rep's from a Po-Be source but, unfortunately, his results are expressed in terms of Po content of the source instead of in terms of neutron flux.

This reviewer, in unpublished work, has indirectly confirmed Dainty's dose values by the use of the plastic tissue chamber, not on the basis of Po content, but on the basis of Dainty's own estimate of the neutron- $\alpha$ -particle ratio. Since the latter was based on the neutron energy spectra of Richards (70) and Perlman (71) there is reason to believe that, within the rather wide limits of experimental error, these spectra are fundamentally correct.

It should be emphasized at this point that the twin ionization chamber method involving the use of  $(\text{CH}_2)_n$  compounds possesses the basic advantage of leading directly to the energy absorbed in "tissue" on account of their similarity of cross-section to neutrons over most the 0.1-10 Mev range (72). The frequently used combination methane-argon does not possess this advantage.

In view of the combinations possible, it is useful to comment on the variation of the parameter  $(J_1 - J_2)/J_1$  when homogenous "twin" chambers are irradiated with uncontaminated neutrons of definite energy. The results,

partly obtained from the original articles (72, 75, 76) and partly calculated by your reviewer, are shown in Table III. It will be seen that the  $\text{CH}_2\text{—CD}_2$  pair is of questionable practical use unless the neutron beam is fairly monoenergetic and "clean." To a lesser extent, the same can be said of the  $\text{CH}_2\text{—CD}$  combination. The  $\text{CH}_2\text{—CH}$  pair offers the highest accuracy if no knowledge of neutron energy is available, but its usefulness is limited to beams contaminated only moderately with photons. When these proportions are reversed the best over-all information is given by the  $\text{CH}_2\text{—C}$  combination.

TABLE III

VALUES OF  $(J_1 - J_2)/J_1$  OBTAINABLE UNDER NEUTRON RADIATION IN "TWIN" HOMOGENEOUS IONIZATION CHAMBERS WHICH HAVE BEEN BALANCED FOR PHOTON RADIATION (SEE TEXT)

Neutron Energy (Mev)	Materials			
	1— $\text{CH}_2$ 2—C	1— $\text{CH}_2$ 2—CH	1— $\text{CH}_2$ 2— $\text{CD}_2$	1— $\text{CH}_2$ 2—CD
.04	.94	.44	—	—
.10	.91	.44	—	—
.25	.90	.44	.615	.75
.50	.89	.45	.45	.65
1.0	.81	.41	.30	.57
2.0	.90	.45	.21	.52
4.0	.82	.46	.17	.47
6.0	.83	.46	.15	.46
10.0	.74	.49	.10	.40

These preliminary calculations point to the desirability of a thorough study of the twin ionization chamber method aimed at assessing its practical limitations with an accuracy greater than it is possible from this cursory analysis. Dainty has already made a start in this direction with the means at his disposal, but access to monochromatic, pure neutron beams is imperative if the matter is to be settled beyond dispute. Moreover, the equivalence of chamber response to photon radiation must be established accurately within wide limits of energy if gross errors are to be avoided. Ultimately, the usefulness of the twin chamber ionization method for the measurement of neutron dose in the presence of  $\gamma$ -radiation, must break down in the presence of high photon contamination because of the high relative biological effectiveness of neutrons ( $\sim 10$ ) and of the difficulties peculiar to the measurement of a small difference between two relatively high currents. Some improvement in the situation may be obtained by the use of photon absorbers, but this simple expedient, requiring the assessment of the effect of the absorbers on the "pure" neutron currents, has not been investigated in any detail.

This state of affairs has led to the use of instruments that are capable of

high discrimination against photons but are, unfortunately, also insensitive to neutrons of energy lower than 200 to 300 kev. By suitable alteration of a thick hydrogenous radiator, Hurst *et al.* (78) have produced a proportional counter, the counting response of which is proportional to dose of neutrons within the energy range 0.3 to 14 Mev. Experiments with neutron fluxes of known energy monitored with the long counter of Hanson & McKibben (79) have confirmed the soundness of the principles underlying its design. However, as described, the instrument has strong directional properties and in practice the correctness of the energy response must be set, paradoxically enough, by means of its weak response to radium radiation. Hurst has attacked the problem further with a "tissue equivalent" proportional counter made of polythene walls and methane gas filling (80). The pulses generated are amplified electronically and integrated by an ingeniously contrived scaling circuit (81) the counting rate of which is proportional to the rate of ionization produced by the recoil nuclei in the gas. Calibration of pulse height is obtained with an internal  $\alpha$ -ray source, and proper adjustment of the bias excludes ionization of electrons, at the price, however, of complete neglect of the low-energy recoils. This device is amenable to current integration, and Moyer (82) estimates that an output of  $3.4 \times 10^{-13}$  amps/cm.<sup>2</sup> with a pulse amplification of  $10^4$  is obtained with a neutron dose rate of 2.79 ergs/gm. (30 mrep's) per 48 hr.

*Scintillation methods.*—Detection of neutrons in the presence of photons has been reported by several investigators who have utilized the higher specific loss of recoil protons for the purpose of discrimination against secondary electrons produced by  $\gamma$ -rays. Various combinations of phosphors and proton producing media have been tried (82 to 86). Discrimination against electrons seems adequate in several cases (84, 85, 87) but only Hornyak (85), having access to monoenergetic neutrons (0.5 to 14 Mev) and photons (1.2 to 17.6 Mev) has been able to prove that discrimination against photons under a wide variety of circumstances can be obtained. His scintillator consists of suitably grained ZnS phosphors properly dispersed in lucite. In view of the fair detecting efficiency and the relative simplicity of construction of this device it seems most urgent that a study of the relationship between counting and dose rates be made with this or similar detectors.

Berlman, at the Argonne National Laboratory, has reported (88) on the application of the "twin" scintillator principle to neutron dosimetry. Preliminary results with organic scintillating solutions of equal electron but dissimilar proton content, have shown the feasibility of obtaining equal photon response by compensating differences in light emission with detector adjustments. Under these conditions the presence of proton recoils caused by radiation from Po-Be and Po-B sources could easily be demonstrated by differences in the pulse height spectra in the two solutions. Since the variation of pulse height with proton energy can be obtained independently, the spectral differences should lead to the recoil proton spectrum and thence, by well known methods, to the neutron energy distribution. Contrasted with pro-



portional counting, this method should permit dosimetry of neutrons of energy lower than a few hundred kev and it should extend somewhat the range of applicability of the twin ionization chamber principle by virtue of its spectrometric property; the latter, however, is unlikely to be as effective as specific ionization as a general basis for discrimination against gamma rays.

*Status of  $W$  and  $p$  for heavy particles.*—The reader will recall that, since Gray's review in 1944 (67), the subject of  $W$  came under review by Bethe (89) in 1950 following the investigations of Jesse and collaborators (90) on  $W$  for  $\alpha$ 's in argon and air. On the bulk of the available evidence, Bethe concluded that: (a)  $W$  is a constant for argon irrespective of the energy and the nature of the ionizing particle; (b)  $W$  should be considered independent of energy for all noble gases, (c)  $W$  in air increases with decreasing  $\alpha$ -particle energy; and (d) there is reason to believe that  $W$  is the same for any one gas for either protons or  $\alpha$ 's of the same velocity. In the interim many reports on the value of  $W$  for  $\alpha$  particles have appeared. The most consistent ones are shown in Table I where both absolute magnitudes, and ratios to  $W$  for air, are shown for purposes of comparison. It should be noticed that these results show satisfactory agreement for many gases with the notable exception of He for which, as Jesse *et al.* have conclusively shown (91), the value of  $W$  is extremely sensitive to the purity of the gas.

Disagreement with Bethe's conclusions has been voiced by some observers. Thus Cranshaw & Harvey (92) report  $\bar{W}$  (air) =  $32.75 + 6.5E_{\text{MeV}}^{-1/2}$  (air) and  $\bar{W}$  (A) =  $27.5 + 1.9E_{\text{MeV}}^{-1/2}$  at variance with the absolute values gathered in the table. This variation of  $\bar{W}$  with energy was surmised by a well-intended but somewhat unconvincing extrapolation from values of  $\bar{W}$  obtained with alphas of 5 to 9 Mev energy. Rossi (93) using alphas from thick uranium sources in several gases obtains instead relative values agreeing with the rest. Objections raised by Hanna (94) seem to have been answered by De Juren & Rosenwasser (95) on the grounds of incomplete ion collection. There remain the exceptions offered by Tunnicliffe & Ward (96) based on ionization by  $H^+$ ,  $D^+$  and  $He^{++}$  (200 to 500 kev) recoils released by neutron bombardment in glass proportional counters of the external cathode type: these workers report  $W(H^+) = W(D^+)$ , but  $\bar{W}(He^{++}) = 1.08 \bar{W}(H^+)$ . In view of the fact that gas mixtures were used, it is difficult to assess the import of their otherwise careful work since both gas impurities and stopping powers are involved.

Bethe's conclusion (c) has also come under scrutiny by Kimura *et al.* (97), who attribute the increase in  $\bar{W}$  in air at low  $\alpha$ -ray energies to the faulty collection of ions at the end of the Bragg curve.<sup>6</sup>

Of definite interest are the values of  $W$  by Bakker & Segré for 340 Mev protons (98). It is somewhat puzzling, however, that their results should have been used so widely for the empirical calculations of  $I/Z$  in Bethe's

<sup>6</sup> The writer, searching for an index of reliability in so many conflicting observations, is inclined to regard with considerable skepticism any value of  $\bar{W}$  obtained with densely ionizing radiation, which is reported without exhaustive investigation of this experimental detail.



formula despite these authors' reservations on the effect of star formation.

Contrasted to the case of  $W$ , for the consideration of which experiment seems to be the only recourse, the vicissitudes of  $\rho$  have been shared also by the theoretical physicist. The unsatisfactory state of affairs of this subject in circumstances of interest to radiobiology, has been reviewed in a scholarly article by Platzman (99) who has considered in detail the factors entering into the accurate determination of stopping power in monatomic and polyatomic gases, in liquids and in solids.

The stopping power of water has been recently studied by de Carvalho & Yagoda (100) who find [at variance with previously published results (101, 102, 103)] that the molecular stopping powers of both  $H_2O$  and  $D_2O$  are identical in magnitude irrespective of the state of the medium. Similarly, experiments by Ellis, Rossi & Failla (104) and Wilkinson (105) show that, within the reported experimental error of  $\pm 2$  per cent the molecular stopping powers for  $Po \alpha$ 's in polystyrene and polythene are respectively identical to those of the gases acetylene and ethylene.

Preliminary announcements from the California Institute of Technology indicate (106), however, that although the energy loss from  $H^+$  and  $D^+$  of the same velocity is the same down to 25 kev, the energy dependence of the stopping cross-sections varies with the gas; moreover, Bragg's additivity law seems to break down for particles of energies below 100 kev.

Relative stopping powers for 180 Mev deuterons in elements ranging from hydrogen to uranium have been reported by Tobias *et al.* (107) in tabular and graphical form. This paper contains also a bibliography of the scattered results reported for  $H^+$ ,  $D^+$ , and  $He^{++}$  particles of high energy.

Although conclusions are difficult to draw in a situation as fluid as this, your reviewer cannot escape the feeling that  $\bar{W}$  is sensibly constant with energy for any given gas but that  $\rho$  may vary considerably for heavy ions in energy ranges frequently encountered in neutron dosimetry.

#### RADIATION PROTECTION

The subject of radiation protection has commanded increasingly wider attention since the advent of nuclear reactors and multi-Mev accelerators. A relatively recent bibliography has been published (108) and a survey of the indices of *Physics Abstracts* of the last four years shows that this subject and radiation monitoring have already assumed the distinction of a separate heading.

This is wholly justified by the need for educating users of radiation in various parts of the world, but should not in any way be construed as an index of technical advancement. Today the subject ranks definitely as an art, not only because of inadequate quantitative biological data on man, but also because of insufficiently developed shielding theory readily applicable to both gamma and neutron sources under the numerous conditions obtaining in practice.

Our comments will be restricted primarily to the latter subject, neglecting

absorption coefficients, more properly treated in other parts of this volume.

The theoretical literature on the penetration and diffusion of photons in thick barriers is relatively profuse (109 to 121) but cannot be considered redundant until relevant experimentation proves the extent of its scattered, empirical applicability. Findings are also available (121 to 128) but comparison with theory is rather scant (129, 130).

White (129) has determined the attenuation of gamma rays from a  $\text{Co}^{60}$  source immersed in a tank of water, and Hayward (130) with the same experimental set up has investigated the secondary electron energy spectrum by means of an anthracene scintillation counter. These workers find that "build up"<sup>7</sup> approaches, at large distances, the asymptotic values predicted by the analytical methods developed by Bethe, Fano and others (114 to 118), whereas, at intermediate depths, the electron spectrum is in good agreement with the predictions of Spencer *et al.* (119, 120) which are based on a computational method involving polynomial expansion of the basic diffusion equation. More recently, Spencer (121) has approached the problem of calculating photon spectra in infinite homogenous media by semi-asymptotic methods and has furnished data for a plane monodirectional beam of 10.22 Mev photons in Pb and 5.11 Mev in Fe. Dixon (131) has observed the attenuation of wide  $\text{Co}^{60}$  gamma ray beams in concrete and in lead. He finds that the "build up" factor decreases with increasing  $Z$ , and that his values are, therefore, understandably lower than White's; no comparison, however, was made with theory.

Many shielding determinations have been reported for a variety of radiations. Attenuation of photon radiation from  $\text{Co}^{60}$ , Ra and x-ray tubes operated in the range 500 to 2000 kv have been reported (122 to 127).

For readers interested in the installations of photon sources of energy below 2 Mev, the *National Bureau of Standards Handbook* Number 41, (132) should be of invaluable help. For installations of higher energy, the forthcoming publication (55), already mentioned, will be equally useful. Some data have already been published by Laughlin (133), and by Laughlin and co-workers (60).

Experiments and calculations covering protection against both neutron and photon radiation from cyclotrons and their "derivatives" have been published by three groups of workers (134, 135, 136) concerned with the design of massive shields of concrete, concrete aggregates and magnetite ore concentrates around these powerful installations.

In conclusion it should be reemphasized, perhaps, that the empirical knowledge available on shielding cannot provide more than a guide to designers of installations of radiation facilities in medicine, industry and research. The art is young in most of its branches and will not gather stature unless

<sup>7</sup> This is the factor by which the values of attenuation obtained by narrow beams techniques should be multiplied in order to obtain the attenuation in wide beams. This factor is the result of multiple Compton processes and shower production in thick barriers.

nourished by exhaustive reports aimed at evaluating design criteria, and by experimental investigations designed to test the various shielding theories that have been proposed.<sup>8</sup>

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## VERTEBRATE RADIOBIOLOGY: EMBRYOLOGY<sup>1</sup>

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Radiobiological studies on embryonic responses have only recently become activated. This delay may have been due to several factors: (a) the relative scarcity and practical difficulties in obtaining material of exact embryonic age; (b) the inadequate information and presumption that the embryo is radiosensitive to a degree and in a manner somewhat different from the adult organism; and (c) prejudicial interest in the adult forms. In spite of these factors it becomes imperative that the effect of ionizing radiations on the vertebrate embryo be studied energetically not only because of the threat of an atomic disaster which would catch thousands of women in various stages of pregnancy, but also because ionizing radiations are being used increasingly both in diagnosis and treatment, even with pregnant women. Radiological information on embryos of all types exposed at specific stages of development is biologically very important. It is the function of the embryologist with radiological training to pursue these studies and interpret the results.

Some 30 to 40 years ago there were some radioembryonic studies, but since the physical conditions were limited and often uncontrolled, the results cannot be reproduced. It will be the purpose of this review to summarize the better controlled experiments of the last several years.

Practically all of the studies reviewed here have dealt with the highly penetrating x- or gamma rays and it may be some time before the embryo is used as a test object for determining any biologically qualitative differences between radiations. Isotopes are used primarily as tracer elements (58), and such studies on the embryo have been made. Those studies which indicate gradients in development, or those which tend to alter the embryonic course of development, will be included.

It is the conviction of this reviewer that factors affecting the gamete which alter the subsequent embryonic development come within the scope of "embryonic effects." Genetic (mutational) effects require large numbers and generations of study. Some of the so-called "lethal mutations," which kill the embryo at one or another stage in development may not be mutations as properly defined. They may be attributed to drastic damage of the entire chromosomal complex of the egg, for instance, consequently leaving for the sperm only its activating function. The biological effects resulting from such high dose irradiation of the gametes should be considered within the realm of embryological effects simply because they are not mutational but

<sup>1</sup> The survey of literature pertaining to this review was completed in February, 1953.

bring about first generation developmental teratologies. Direct effects on the embryo follow much lower levels of exposure.

Finally, it would be unwise to group together all vertebrate radioembryonic effects, particularly when this would include the somewhat poikilothermic fish and amphibia, with the homoiothermic birds and mammals. Such a plan would also consider simultaneously those forms with 21-day and 9-month gestation periods. It is therefore proposed that these groups of vertebrate embryos be treated chronologically and independently of each other. Such summary statements as appear to be justified will be made as general conclusions.

### FISH

Fish gametes and embryos have not proven to be very satisfactory experimental material in radiobiology. Following the original work of Opperman in 1913 (3) there were relatively few studies until 1948 when two papers on the salmon and one on trout appeared. Foster and co-workers (18, 19) found that x-irradiation of the parent trout from 50 r to 2500 r did not delay spawning appreciably. The x-rayed gametes did not recover, even with enforced delay in the spawning time following exposure. Developmental abnormalities included deficiencies, disproportionate growth and differentiation, twinning, spina bifida, and cyclopia. An exposure to 500 r of the parent fish caused slight retardation in developmental rate, and many failed in the closure of the blastopore.

Welander *et al.* (64) found that salmon embryos in the "eye" stage could tolerate 2500 r and would hatch and appear normal for some 4 weeks and would then suddenly die (30 to 51 days). This dose arrested the development of cutaneous pigment, growth in both length and weight, and the vascular development to the fin rays and other organs. Just before death there were severe vascular disturbances, loss of vitality, paralysis, and edema as well as other abnormalities. Doses of 500 r to the embryos caused some of these abnormalities, but to a much lesser degree, and mortality was only slightly greater than for the controls. The gonads and the hematopoietic tissues of these developing embryos seemed to be the most sensitive. A dose of 250 r inhibited the development of the primordial germ cells and caused temporary retardation of the development of hematopoietic tissue of the anterior kidney. The general syndrome appeared to be the same as for embryos of other groups of animals but differed in the time of appearance and in the interval between irradiation and death. Bonham *et al.* (7), using the fingerling Chinook salmon, found that 250 r increased mortality, 500 r affected weight, 750 r blood development and 1000 r altered length.

One of the main advantages of the fish embryo for radiobiological studies lies in its transparency so that developmental changes may be observed without sacrificing the animals. Further, many of these poikilothermic forms have a slow rate of development so that they may prove valuable in analyzing any changes that occur between the exposure and the appearance of

the definitive radiation syndrome. It is hoped that both marine and fresh water fish embryos will be used more aggressively in radiobiological studies.

#### AMPHIBIA

*Gametes and early development.*—The "Hertwig Effect" is being revived in current radiobiological research with amphibian material and should be defined briefly. Hertwig (22) was one of the first to demonstrate that with increasing exposures of sperm (or eggs) to ionizing radiations, there were increasing abnormalities among the resulting embryos. However, if exposure was extended well beyond the level which produced 100 per cent abnormalities in the embryo, they again achieved what appeared to be normal embryos. This radiation neutralization of the sperm's genetic influence, but retention of its activating ability so that normal eggs could be (parthenogenetically) stimulated, is known as the "Hertwig Effect." By cross fertilization between species, Rugh (40), and Rugh & Exner (41) further confirmed this effect. The fact that irradiated bullfrog sperm caused normal leopard frog eggs to develop to the early tadpole stage proved the "Hertwig Effect" since the control crosses between unirradiated gametes never reach gastrulation. The embryo in such instances has but half of its normal complement of chromosomes (is haploid) and generally does not survive very long.

Briggs *et al.* (9) cytologically examined many *Rana pipiens* eggs fertilized by x-irradiated (65, 300 r) *R. pipiens* and *R. catesbiana* sperm and found that at least 86 per cent were definitely haploid and less than 1 per cent were diploid. Cleavage in such eggs was normal but delayed. After removal of the unirradiated female (egg) nucleus from such inseminated eggs, leaving only the x-irradiated sperm in the normal yolk and cytoplasm, the eggs did cleave, although there was further delay. Upon cytological examination many of the blastomeres were found to be without any chromosomal material at all. This seems to be evidence that the mechanisms controlling cleavage may be achiromatic. The investigators seemed to feel that the irradiated sperm did contribute something toward the kinetics of cleavage, even though the chromatin was functionless. The cells containing x-irradiated chromatin were generally bunched to one side of the partial blastula at 24 hr., with the chromatin-free cells toward the other hemisphere. Shortly the cells began to disintegrate with the chromatin-free cells breaking down first. Achromosomal cells transplanted to a normal host environment failed to survive any better than in their original early partial blastula.

Duryee (16, 17), with very refined micromanipulation techniques, has isolated normal and irradiated chromosomes and has transplanted them, sometimes along with the cytoplasm and the yolk, with the following findings: (A) Ovarian eggs from salamanders or frogs, when x-irradiated from 500 r to 60,000 r in graded steps, show progressive stages of pycnosis. After 3000 r some 98 per cent of the small eggs showed intranuclear damage within 10 days. (B) Criteria for radiation injury are: fragmentation of the chromosomes, loss of lateral chromomere loops, colloidal changes in the nu-

cleoli, sol-gel changes in the intranuclear spindle substance, and localized cytoplasmic flocculation. (C) Nuclear components *in situ* were not equally radiosensitive. Nucleoli were evacuated at 1000 r; chromomere loops were dissolved after 2000 r; chromonemata were broken at 3000 r, and spindle substance was solvated at 50,000 r. When these components were individually isolated from their cytoplasmic environment and then x-irradiated, they proved to be markedly radioresistant. (D) Exposures to low temperatures (5°C.) delayed nuclear injury from x-irradiation up to 18 days but did not prevent eventual pycnosis when the animals were brought to 23°C. Higher temperatures accelerated the appearance of radiation injury. (E) Isolated egg nuclei are highly resistant to x-ray damage as compared with the nuclei *in situ*. (F) Microinjections into nonirradiated eggs of cytoplasmic material from irradiated eggs induced typical nuclear radiation damage. Chromosomal and nuclear injuries were produced by exposure of isolated normal nuclei to x-irradiated cytoplasmic brei. (G) Cellular radiation damage is caused by: (i) radiochemical changes in the cytoplasm; (ii) accumulation of metabolic toxins from irradiated nuclei; and (iii) rapid transmission of toxic substances into the nucleus at usual laboratory temperatures.

Rollason (39) x-irradiated eggs from *R. pipiens* at different stages of maturation and fertilization and found that the newly fertilized egg was the most radiosensitive, followed by the uterine and then the ovarian egg. The 50 per cent mortality level for newly fertilized eggs was 150 r, although some surviving eggs reached gastrulation even after an exposure of 1000 r. Obviously, in the fertilized eggs both gametic nuclei were exposed. Her findings seemed to indicate that the frog's sperm are more radiosensitive than are the eggs, as measured by the effect on embryonic development. The cleavage rate and pattern were not affected by irradiation of any stage of egg maturation even to 41,600 r, and the types of developmental abnormalities following irradiation of the unfertilized egg were the same as those following exposure of the sperm alone. A delay of 24 hr. between exposure of the egg and fertilization gave no evidence of recovery.

*The embryo.*—Embryos of the frog, *R. pipiens*, were exposed at developmental stages 18 to 25, to x-irradiations from 10,000 r to 50,000 r and were found to survive from 1 to 6 days [Rugh (43)]. The later stages of this series were somewhat more radiosensitive than were the earlier ones, possibly attributable to the development of excretory and respiratory functions. Growth was impeded by 10,000 r and abruptly stopped by 50,000 r. A single exposure of 10,000 r killed all embryos (tadpoles) within 6 days. Exposure of embryonic, stages 18 through 25, to 50,000 r, did not kill any within 24 hr. but all were dead within 3 days. Embryos exposed at stage 18 generally developed lordosis, those at stage 21 developed belly edema, and those at stage 25 acquired large head blisters, with no lordosis or belly edema. Edema occurred at lower doses and earlier embryonic stages, 18 to 20, in the belly region as a result of the accumulation of fluid in the coelomic spaces, adjacent to the newly functioning vitelline veins. At later stages, 20 to 22, the same

exposure caused edema of the head, producing irregular head shapes because of fluid in the anterior lymph spaces. Finally, edema formed blisters on the head, stages 23 to 25, associated with the respiratory (gill) structures [Rugh (43)]. These varying regional sensitivities were explained on the basis of heightened activity (differentiation) at the time of exposure. The lordosis, for instance, was caused by exposure at a time when the central nervous system and central axial skeleton were being laid down and the head swelling at a time when the anterior lymph spaces were forming.

Carrying this type of study further, Rugh (42) exposed *Amblystoma punctatum* larvae measuring 2.2 cm. in total length to a single large dose of 15,000 r x-rays and examined the larvae for histopathological changes. He found that mitosis was abruptly stopped in all cells which had not started the process and those which were in mitosis became pycnotic. Cartilage and muscle were the most developed and the most resistant tissues, there being no evidence of damage to the intercellular matrix of the cartilage or to the myoplasm or myofibrillae of the muscle. The neuroblasts of the central nervous system and the related sense organs were the most radiosensitive. Neuroblasts were sloughed off into the brain cavity and neurocoele. The nervous tissues were the most active at the time of exposure. The scale of tissue sensitivity in the embryo was thus proven to be quite different from that of the adult, particularly with respect to the neuroblasts of the developing nervous system.

Certain organs in the developing amphibian embryo are especially sensitive to ionizing radiations, but when transplanted to the healthy environment of a nonirradiated host have been demonstrated by Perri (38) to exceed their life expectancy in their original environment. In some instances the transplanted eye, normally succumbing in the irradiated embryo, lived as long as the host into which it was transplanted. The author concluded that the death of irradiated embryos is attributable to the death of certain especially radiosensitive organs or organ systems indispensable to the life of the embryo, "because those conditions fail that render possible the life of that unity of a superior order which is represented by the organism in its entirety." The reverse transplantation, from normal donor to irradiated host gave no indication of damage from the surrounding irradiated tissues to the normal rudimentary organ.

Czech *et al.* (14) used the cornea of the salamander larva to compare the biological effects of fast electrons and of x-rays and concluded that there was no qualitative difference produced by the two kinds of rays.

Brunst & Sheremetieva-Brunst (13) spot x-rayed from 2000 to 4000 r the lower jaw of 20 to 60 day-old salamander larvae and found that the enamel epithelium disappeared in the exposed developing teeth and that the surrounding tissues were devoid of mitotic phases. New teeth never developed even after a period of one year, so that this treatment permanently destroyed the mechanism for tooth formation and tooth maintenance in those larvae.

Stimulated by the findings of Patt & Swift (37) that adult frogs exposed



to 9000 r died within two weeks but if kept at 5–6°C., survived for 60 days with very low mortality, investigators have turned to the poikilothermic amphibia to determine to what extent low temperatures during and after irradiation might alleviate or postpone the expected syndrome. Allen *et al.* (4) found that so long as *R. catesbiana* tadpoles were maintained at a temperature of 0°C. to 5.5°C. the destructive effects of prior x-irradiation in the normally sensitive hematopoietic cells was very slight. They proved that refrigeration during irradiation did not prevent injury to the formative blood cells in tadpoles subsequently kept at normal temperatures. LaHam & O'Brien (33) reported contrary findings with *Amblystoma maculatum* larvae measuring 22 mm. in total length. They found that the metabolic level at the time of irradiation, controlled by temperatures of 2°C. and 33°C., determined whether the larvae exposed to 15,750 r were to die in 3 days or in 1 day, even though all were kept at room temperature following the exposure. They also claimed that the histopathological damage of the brain and eyes was less in those exposed to x-rays at the lower temperature. This should be investigated further.

Allen *et al.* (3, 5, 6) using the hematopoietic cells of the *R. catesbiana* tadpole as the test object, and the LD<sub>50</sub>/30 days for the tadpole as 10,000 r, found that an exposure of 500 r caused very extensive destruction. However, it was the postirradiation temperature that determined the rate of destruction of the hematopoietic tissues and below 13°C. the breakdown was very slight. If a low temperature was applied for several days and then the tadpoles were transferred to a high temperature, the rate of destruction of the hematopoietic cells changed to the level characteristic for the higher temperature. There was little if any recovery during the low temperature period, only a delay in the destructive processes. They pointed out that irradiation of hematopoietic tissue to 500 r produces injuries that may remain invisible for some time, awaiting reactions or changes in the cells, particularly mitotic changes. In a further study [Schjeide & Allen (54)] the metabolic activity and rate of mitosis were emphasized as the factors controlling the expression of radiosensitivity. "We find that the tadpole hematopoietic tissue appears to be susceptible to 500 r in direct correlation with the amount of cell division allowed to proceed, following the irradiation period. Cells in prophase at the time 500 r x-irradiation is applied are destroyed directly." Cells held in late prophase by colchicine are destroyed by 500 r x-irradiation (55). Also "Our evidence seems to indicate that the primary damage is inflicted in a very high percentage of the haematopoietic cells at the time of irradiation, but this damage is not visible as destruction until these cells begin to divide." The major thesis is simply that the rate of mitosis is proportional to the temperature and that x-irradiated cells are destroyed as they proceed to prophase and hence the rate of destruction is increased with an elevation of temperature. However, at excessive exposures of 10,000 r the amount of hematopoietic cell destruction in any given period exceeds cell division. More recently Allen *et al.* (1, 5, 6) were able to detect graded destruction of hemato-



poietic elements in the anterior kidneys of *R. catesbiana* tadpoles with doses from 25 r to 10,000 r. With 250 to 750 r x-rays mitotic figures were rarely seen before the fifth day post-irradiation. Higher doses resulted in lower division rates. After exposure to 1000 r all of the hematopoietic cells had ceased to divide by the thirtieth day. Gojmerac & O'Brien (20), using larvae of *R. pipiens* and *R. catesbiana*, further confirmed the findings that the post-irradiation temperature could regulate, to some extent, the onset of the histological effects of x-irradiation.

Allen *et al.* (6) found that anoxia markedly reduced the immediate cell destruction in tadpoles following x-irradiation, whether the anoxia was applied during or after the exposure. Anoxia also reduced the colchicine effect, but in either case, its method appeared to be by delaying the process of mitosis. Anoxia did not prevent destruction, but rather seemed to delay its onset.

The amphibian tadpole has long been used as an assay object in experimental endocrinology for thyroid and pituitary hormones. Allen *et al.* (2) report that when the pituitary gland is transplanted from recently metamorphosed toads (*Bufo boreas*) to immature tadpoles of the same species there is the usual acceleration of metamorphosis. Such pituitaries, previously exposed in the donors to x-rays from 1000 r to 20,000 r and then transplanted to normal tadpoles, likewise accelerated metamorphosis and the shedding of larval cuticular teeth. This indicated that the pituitary gland of recently metamorphosed toads had a survival factor some 50 times greater than did the hematopoietic tissue, probably resulting from the special vulnerability of the mitotic cells in the hematopoietic tissue. Allen further communicates: "We are well aware of the practice of irradiating the pituitary gland in treating gigantism and acromegaly. The apparently favorable results might be attributable to injury to the blood vessels, extrinsic and intrinsic, thus reducing the blood supply." (Personal communication).

Local exposures to x-rays of 1000 r or more inhibited the process of tail development in axolotl larvae of 5 or 12 days posthatching age (11). Some 35 to 40 days after exposure Brunst differentiated between zones of inflammation (acute primary reaction), zones of stimulation (overcrowded cells in mitosis), and zones of inhibition (absence of mitosis). He found giant polyblast-macrophages which were described as phagocytizing those cells which were damaged by irradiation. By 85 days all signs of the so-called acute primary reaction were gone and the surviving cells had recovered their normal appearance but had lost their capacity for cell division. In some instances, a secondary tail grew from the dorsal and more proximal portion of the original tail. It was larger than the primary tail, but never attained the size of a normal tail. In another experiment Brunst (12) locally x-rayed with 750 to 8000 r the limbs and the lumbo-sacral region of axolotl larvae measuring from 17 to 23 mm. in total length, and studied the effect on the pelvic girdle and limb development. All doses used inhibited limb development and there was a total absence of the pelvic girdle. Even in cases of scattered irradi-

ation ("through improper placement of the animal during irradiation") there was abnormal growth of the exposed limb area. There was rather complete differentiation of skeletal and other tissues, but without mitotic figures. Some development of a limb occurred if irradiation was imposed after the initial appearance of its rudiment. Brunst (11) says: "It is possible that x-rays, in general, prevent the type of differentiation which is intimately related to the process of cell multiplication. However, x-rays may not have such an influence upon the type of differentiation, which occurs without great mitotic activity but with a simple continuation of differentiation of the rudiment." If Brunst implies various types of differentiation, there will be many to take issue with him. After a lengthy latent period (42 days) Brunst claimed that a hyperdevelopment of new limbs occurred as a result of a late secondary stimulating effect following the original single exposure to the lumbo-sacral region. There was ultimately complete normal recovery to a "stable state" which continued for an unlimited time.

*Regeneration in larvae.*—Ionizing radiations have been used in studies on regeneration because of their known effects on embryonic or highly proliferating tissue, and regenerating blastemas are usually considered to be basically similar to such tissues. Certainly the cut surface of an embryo or young adult organism provides cells which are physiologically different from adjacent cells and which may conceivably have different radiosensitivities.

From 1933 to 1950 Brunst and his wife, Sheremetieva-Brunst, published some 21 papers on radiation effects on regeneration of amphibian parts, and these works have been summarized by Brunst (10). He reported that post amputation irradiation caused an arrest and then a rapid reduction in the size of the potential regenerate, and this he attributed to the presence of what he called the giant cells of the inflammatory process. "The tissues weakened by irradiation are destroyed by the macrophages through phagocytosis and lysis." Irradiation prior to amputation of an adult limb caused no reduction because "adult organs consisting of differentiated cells do not show the acute reaction," but they do regenerate. The local application of x-irradiation caused local destruction of the regenerative capacity without affecting adjacent areas, even though they were distal to the irradiated region. A normal regenerating blastema transplanted into an irradiated limb resulted in a normal regenerate, and an irradiated blastema failed to develop even when transplanted into a normal site. This is because the regenerating blastema is formed from local cellular elements.

Brunst (10) further states that an x-ray dose which suppresses cell division is much lower than the dose which kills the cells outright. These sublethal doses may prevent growth, regeneration, and development. However, organs which consist of x-ray inhibited mitoses, will still persist for a long period in what he calls a "secondary stable state." He believes that differentiation can go on in spite of the radiation-suppression of cell division, a concept rather difficult to accept. Ontogenetically, differentiation is accom-

plished just prior to or during the process of cell division. It is difficult to see how a cell once differentiated can become otherwise differentiated without an intervening process of dedifferentiation and redifferentiation through mitotic activity.

Thornton (59) immersed *Amblystoma larvae* in beryllium nitrate solution for 2 min. and then amputated their limbs. He also exposed the blastema to beryllium to find in both cases that the treatment did not prevent further cell proliferation. However, beryllium invading the blastema did interfere with its differentiation.

#### THE CHICK

Karnofsky *et al.* (32) claimed that Roentgen rays had both an acute and a delayed toxic effect on the chick embryo. The acute effect was expressed in death within 24 hr. after exposure and the delayed effects resulted in death without 10 days. In embryos of 8 days or older the acute effect depended upon the dose rate above 5 or 10 r per min. and was relatively independent of the total dose above 800 r. There was an increased sensitivity to this acute effect between 3 and 7 days, with maximum sensitivity between 8 and 10 days, and more resistance after twelve days. The delayed effects were cumulative. Acute death studies indicated an LD<sub>50</sub> of about 2000 r for the 2-day embryo, 700 r for the 8-day stage, and a slight rise to 900 r by 16 days. "The effects of Roentgen rays are still cumulative to produce delayed deaths at a dose rate of 0.55 r per min." (32). The delayed death syndrome included vascular injury and hemorrhage, edema, necrosis of the liver, and stunting of growth. Developmental abnormalities were most obviously in the beak, limbs, head, and eyes.

Schneller (56) studied the effect of direct irradiation of the chick embryo in contrast with the effect of irradiation of the extraembryonic areas and the yolk only. She chose the 33-hr. stage which has no formed vascular components and the 60-hr. stage in which there is a beating heart connected with a closed vascular system that is largely extraembryonic. By means of lead shielding the embryo she was able to expose only the extraembryonic areas and to compare the effects with whole egg exposure.

She found that an exposure of the whole egg to about 450 r x-rays at the 33 hr. stage was the LD<sub>50</sub> dose and it took 900 r to kill all of the embryos within 48 hr. If, however, she shielded the embryo with lead, exposing the yolk only, the LD<sub>50</sub> dose was between 1500 to 2000 r and to kill all embryos it took about 5000 r hard x-rays.

In contrast with these findings on the 33 hr. stage the 60 hr. embryo had an LD<sub>50</sub> of about 550 r and an LD<sub>100</sub> of about 700 r. When the embryos were shielded with lead it took only 800 r to kill half of them and something more than 1500 r to kill all of them. Therefore an embryo 27 hr. older showed a measurable increase in sensitivity of its extraembryonic areas to x-irradiation. The major structural difference related to the actively developing and extensive extraembryonic vascular bed.

After establishing 900 r as the completely lethal dose for the 33 hr. embryo, Schneller determined that by 1 hr. postirradiation there were no discernible histological effects; by 3½ hr. there was a sloughing off of neuroblast cells into the developing brain cavity and by 21 hr. postirradiation there was a definite increase in the number of degenerating cells, including giant cells in the developing heart and head mesenchyme. By 27 hr. multinucleated giant cells and frequent pyknosis were observed and after 45 hr. there seemed to be a decrease in the abundance of loose cells within the body cavity, possibly attributable to some phagocytosis.

Using the method of chorio-allantoic grafting, Schneller excised organs from embryos which had received previously demonstrated 100 per cent lethal exposures to x-rays and transplanted these organs to the chorio-allantois of normal unirradiated hosts. Both the optic vesicles and the limb buds from early embryos, following exposure to 1000 r x-rays, survived and developed in a manner comparable to control grafts suggesting that these organs were not responsible for the lethal effects on the whole embryos and that they, at least, could tolerate lethal doses to the embryo.

This type of study points up the fact that lethality of an embryo or organism may be determined by specific high sensitivity of a single vitally important organ system; that the developing blood vascular system is definitely radiosensitive; and that probably many organ systems are relatively radioresistant but may be carried to death by more sensitive systems within the same organism. Examples are the limb bud or optic vesicles which, when transplanted from a moribund embryo, will survive in a healthy environment. Nevertheless, the embryo as a functional, integrated whole, cannot survive if its vitally important and most radiosensitive part is x-ray-insulted.

Tobin & O'Brien (60) agree with Schneller (56) that the wall of the developing chick brain is very radiosensitive, stating that there were also indirect effects of ionizing radiations on the mesencephalon. These indirect effects were basically the same but were more delayed and generally less severe.

Warren & Dixon (15, 62, 63) in a thorough histopathological study reported the effect of continuous  $\beta$ -irradiation by injecting  $P^{32}$  into chick embryos. They injected from 115 to 1050  $\mu$ c. and found that 90 per cent of the isotope, injected into the yolk on the fifth day of incubation, was taken up by the embryo and at hatching was largely found concentrated in the bones. There was a general but equal retardation of growth of both males and females resulting from this concentrated  $\beta$ -irradiation, possibly attributable to the fact that after  $P^{32}$  was incorporated into the developing bone it could not readily escape. The developing gonads were also found to be very radiosensitive to  $\beta$ -radiations. The primitive sex cells of either sex were the most radiosensitive, and the spermatogenic cells were five times as sensitive as the somatic testicular cells. The potential ovary showed degrees of damage depending upon the amount of radiation. The ova became more radio-

resistant as they matured. While the somatic cells of the gonads were less sensitive than were the germ cells, their growth too was inhibited. In none of the potential male birds,  $P^{32}$  irradiated during incubation, did the secondary sexual characters develop during the 60-day observation period. Bone growth was definitely retarded and the cartilage cells of the epiphyses were found to be more radiosensitive than were either the osteoclasts or osteoblasts. Following the loss of  $\beta$ -radiation by degradation the bones remained shorter and lighter. They resumed growth but remained retarded, so that the newly hatched chicks were well-proportioned but small. The authors also report that smaller doses of  $P^{32}$  (47 to 300  $\mu$ c.) inhibited maturation of the immature hematopoietic cells and reduced their mitotic activity. A large dose caused a fatal anemia. Regardless of dose, the bone was affected and the mitotic activity of its marrow cells was inhibited. The changes following small doses was reversible so that when the irradiation was reduced there was a return to the normal activity. The lymphoid tissue, particularly the thymus, was radiosensitive and reacted within 48 hr. and until the time when most of the  $P^{32}$  was concentrated in the bones. Only the gonads showed sensitivity comparable to the lymphoid tissue. The peripheral blood counts followed the expected pattern, with an initial lymphopenia followed by rapid recovery. Then there was a granulocyte drop and finally an erythrocyte depression which recovered faster than did the granulocytes.

#### THE MAMMAL

*The mouse.*—When Russell & Russell (47, 48) x-irradiated the pre- and postimplantation stages of pregnant mice they found that the earliest stages were the most radiosensitive. Females x-irradiated with 200 r on days 0.5 to 2.5 produced only about 20 per cent as many living embryos as did the controls. Those exposed on day 3.5 produced 31 per cent and those exposed on day 4.5 produced 57 per cent as many as did the nonirradiated controls. Those irradiated at 2.5 days and 3.5 days were apparently killed before implantation, while those irradiated at other times may have been killed after implantation. Total litter death may have resulted from radiation effects on the mother in addition to direct lethal action on the embryos.

Russell (49, 50) reported further analyses of embryonic exposures. She found that exposure between days 0.5 to 4.5 (and possibly 5.5) accounted for the high death rate but there was 98 per cent normality among the survivors; days 6.5 to 13.5 accounted for very little prenatal death but a high incidence of abnormalities among the survivors at birth; in cases of irradiation between day 14.5 and normal birth there was no prenatal death (even with 300 r) or visible abnormalities at birth. Some abnormalities did appear later in life, such as cataracts, hydrocephalus, and skin defects. The peak incidence of natal death occurred in radiations on days 9.5 and 10.5. She listed some 13 types of gross abnormalities that appeared at birth in embryos irradiated between days 6.5 and 13.5. These abnormalities included: microphthalmia,



coloboma, narrow iris, vaulted cranium, snout and nostril abnormality, cranial blister, narrow head, open eyelids, spina bifida, small or imperforate anus, hydronephrosis and/or hydroureter, reduction in tail length, abnormalities in tail shape, overgrowth of feet (polydactyly), digital reductions (oligodactyly), and limb abnormalities. In many cases sensitivity was found to occur at a period when there were most rapid changes in the primordia. However, she made the statement that "Sensitivity is not predictable from known facts of descriptive embryology since certain sensitivities occur before the appearance of known primordia." With regard to the abnormalities, Russell believed that sensitivity may not be limited to one stage for a particular organ but that there may exist some lesser degree of radiosensitivity at another stage or stages. Increasing exposure did not accentuate the abnormality (e.g., never more than 6 toes) but there was a higher incidence of any specific abnormality with higher exposure to the fetus of the same age.

Certain other conclusions of Russell are worthy of mention: There was no evidence of any shift in the sex ratio among the survivors, and since irradiated mothers could nurse litters from control mothers, there was no evidence of inability of mothers to care for their young and they did not contribute to the maldevelopment of the suckling young. The irradiation effects were therefore presumed to affect the embryo directly.

In a clever use of hybrid mice, to detect certain skeletal variations, Russell & Russell (51) found that if mouse embryos were irradiated at 8.5 days there was maximum incidence of posterior shift in the thoraco-lumbar border, although animals exposed during the 24 hr. prior to or after this peak also showed some such tendency. With as low a dose as 25 r to certain hybrid embryos at 8.5 days there was an increase in the development of the fourteenth rib, and this reaction was accentuated with increased exposures on the same day. They stated that in strains where there is no natural variability, characters were found to be considerably more resistant to radiation-induced shifting than in other strains.

Russell *et al.* (52) studied the possible protective effect of hypoxia on those abnormalities induced in the mouse fetus by x-irradiation at 11½ days of embryonic age. They found that hypoxia itself had no effect on the embryo but, combined with x-irradiation, it had a marked protective effect against damage with respect to all the characters previously shown to be affected by irradiation on that day. These characters included birth weight, viability, tail length and shape, and limb development.

Russell & Russell (53) reviewed the detailed studies on irradiation of the fetal mouse and endeavored to draw analogies for the human fetus. They again pointed out that fetal sensitivity was correlated with the high rate of change in the developing organism, and that when the limb buds, for instance, were embarking on their active growth, irradiation would tend to cause oligodactyly. The forefeet were radiosensitive at an earlier date than



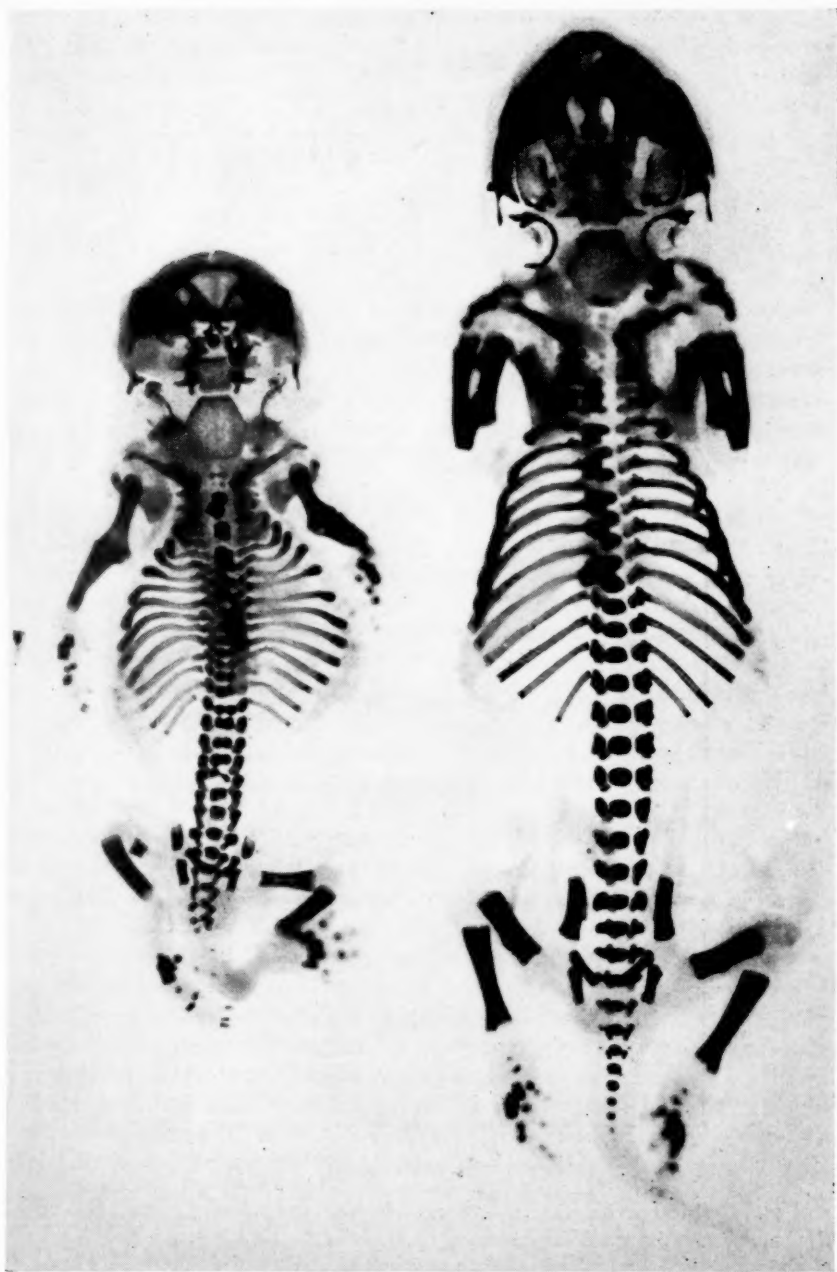


FIG. 1. Mouse on left x-irradiated (300 r) in utero at  $10\frac{1}{2}$  days of embryonic age, control on the right. Hardly a single normal bone in the irradiated mouse at birth. Age of exposure estimated as comparable to four weeks for the human embryo. [Courtesy Russell & Russell (53)]

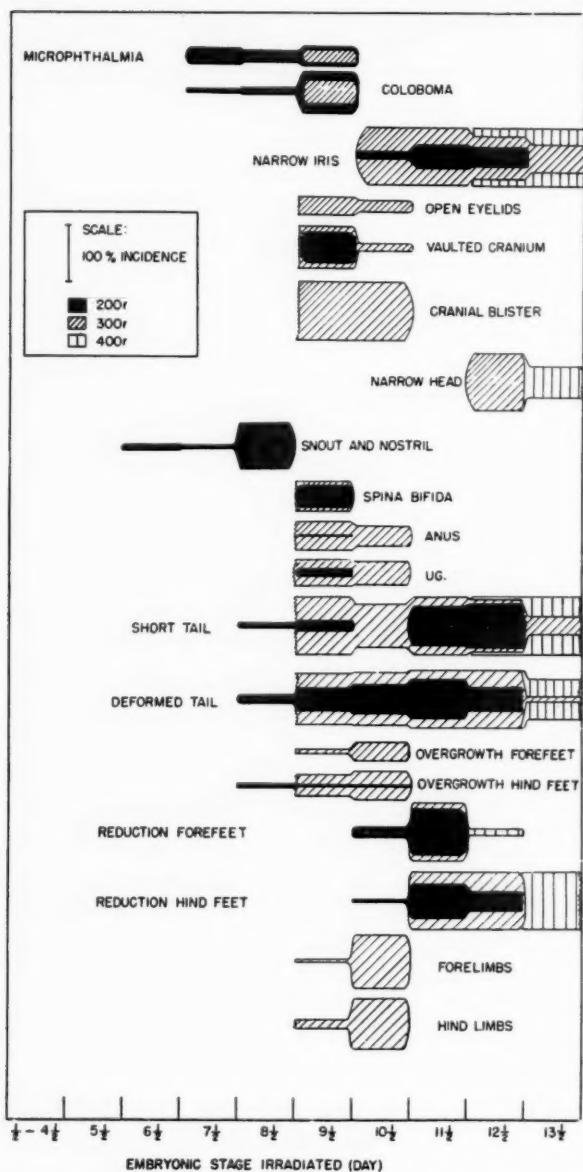


FIG. 2. Critical periods during embryonic life for production of specific abnormalities in mice, the abnormalities described by Russell (49). Both percentage of incidence of abnormality and magnitude of dose required to produce the abnormality are indicated. The wider and more heavily shaded a band, the greater the sensitivity. [Courtesy Russell (49)]

the hindfeet simply because of a time difference in the initiation of development. They listed some 22 characters which have been reported in the literature as being attributable to x-irradiation of the human fetus, many of which they had described as similarly caused in the mouse fetus. However, when trying to homologize mouse and human fetal development they say:

"Time intervals in human prenatal development, which spans thirty-eight weeks, and in mouse development, which is completed in less than three weeks, are not directly proportional. For example, the first one-fourth of mouse prenatal life is equivalent to only the first one thirtieth of that for man."

Otis and his collaborator (35, 36), by using some 80 cross references, obtained a rather smooth curve for comparable stages of mouse and human fetal development. They conclude: "Critical periods for the majority of gross abnormalities in mice occur at a time which, in man, corresponds to the second to the sixth week of gestation" and doses high enough to produce developmental abnormalities do not necessarily cause abortion or prenatal death.

Finally, Rugh (46) x-irradiated pregnant mice to 50 r per day for 6 days beginning on the fourteenth day of gestation so that the accumulated dose before birth was 300 r. This did not prove to be lethal to any of the fetuses, and the young were maintained, along with nonirradiated controls, for a period of six months. The sexes were kept separate to prevent reproductive stimulation of the gonads or other endocrines, and at 6 months the mice were tested for fertility. Roughly two-thirds of all of the offspring were made sterile by this treatment, with slightly greater sterility among the males but a greater number of first generation teratologies from the females. All irradiated males showed some testicular damage, and it was histologically determined that if 40 per cent or more of the seminiferous tubules contained maturation stages, the mouse was fertile. Completely sterile males had testes with less than 10 per cent of the tubules containing maturation stages. There was a relative increase in the interstitial tissue of the sterile testes. The variations in sterility among males of the same litter were attributed to slight differences in stage of development of the gonad primordia at the time of exposure.

Studies on the distribution of radioiodine from a subcutaneous site through the placenta to the mouse fetus have been made by Speert *et al.* (57) and they found that iodine was concentrated in the fetal mouse thyroid by the sixteenth day of gestation but not before. This time corresponds to the time when the fetal thyroid first acquires follicles. They found that neonatal growth was retarded in young born to mothers injected with 200  $\mu$ c. of radioiodine on or after the seventeenth day of gestation, and that later reproductive activity of the female offspring may have been impaired. Many of the offspring thyroids later became fibrotic, with compensatory hyperplasia and adenoma formation. Ultimately colloid goiters developed. By 9

to 12 months about a third of the offspring developed chromophobic adenomas of the pituitary glands, so that the authors advise against the use of radioiodine in treating pregnant human patients after the first trimester, if the therapeutic objectives can be attained by other means.

Rugh (44) studied radioiodine injection of the mouse as it affects the nursing young at 3 days postparturition. The act of nursing tended to drain  $I^{131}$  from the mother, beginning as early as 8 min. postinjection. The mammary channel therefore became an accessory excretory channel for the mother, protecting her to some extent against  $I^{131}$  damage of her thyroid. In a histopathological study of the effect of maternally derived  $I^{131}$  on the nursing young, it was found [Rugh (45)] that doses of radioiodine to the mother at thyroid-ablation levels did not ablate her thyroid nor those of her suckling young, indicating a dilution of the effect by virtue of the suckling process. However, after 10 months the young did show thyroid damage and, with higher doses to the mother at nursing, these young at 10 months developed increasingly large anterior pituitary adenomas, often with hemorrhagic masses. A dose of 5  $\mu$ c. of  $NaI^{131}$  delivered to the suckling mouse at 3 days of age was found to be histologically damaging to both its thyroid and pituitary glands. It was estimated that the thyroid of the 3-day mouse was about three times as sensitive to radioiodine as was that of its mother. The damage to the pituitary was attributed to partial-ablation of the thyroid by radioiodine inducing compensatory development in the anterior pituitary gland. Studies in progress indicate that radioiodine passes readily through the placenta to the mouse fetus and affects its endocrines and gonads to a degree related to the dose injected into the mother. The sensitivity of the fetal tissues, as measured by histopathological changes up to 18 months, indicate that the fetus is at least three times as radiosensitive as is its mother.

*Rat.*—Haskin (21) who used nitrogen mustard (0.5 mg. to 1.0 mg. per kg. of  $HN_2$ ) injections in the pregnant rat on the thirteenth and fourteenth days of gestation, induced marked gross abnormalities in the fetuses detected before the time of birth. Since nitrogen mustards are known to have effects somewhat similar to those of x-rays, namely inhibiting interphase mitosis and the active proliferation of cells, Haskin listed some seven common abnormalities and stated:

"The gross resemblance between fetuses bearing anomalies resulting from abnormal genetic make-up, exposure to ionizing radiations, and nitrogen mustard treatment may be resolved in terms of a general inhibiting action of all three agents"

and

"the generalization of Bergonie and Tribondeau that the sensitivity of cells to radiation varies directly with their reproductive capacity and inversely with their degree of differentiation obtains as well for the mustards."

With respect to x-irradiation of the rat fetus, Warkany & Schraffenberger (61), who were the first to use x-rays to determine the critical periods in de-

TABLE I  
REPRESENTATIVE MALFORMATIONS PRODUCED BY IRRADIATION  
OF RAT FETUS WITH 100 R\*

Day of Irradiation	Organ or Region Affected	Incidence Per Cent
8	None	0
9	eyes	90
	brain	45
	aortic arches	27
	heart	27
	spinal cord	18
	situs inversus	18
	urinary tract	5
10	eyes	75
	urinary tract	25
	brain	11

\* Wilson, Brent, Jordan (72).

velopment, repeated the earlier experiments of Job *et al.* (31) but used a larger number of rats, a greater fetal range and more thoroughly controlled techniques. They described the skeletal abnormalities occurring after fetal irradiation between the tenth and sixteenth days of gestation. These included defects in bones of the skull, cleft palate, mandible, malformation of the ribs and bones of the appendages. They definitely related the time of fetal irradiation to the pattern of the abnormalities produced. At first they thought irradiation on the thirteenth day produced abnormalities that could be confused with those produced by a deficiency in riboflavin, but upon proper clearing and further study a distinction could be drawn.

The first of a series of studies by Wilson and his co-workers (66, 67), in 1949, dealing with the effect of x-irradiation on the rat fetus, described

TABLE II  
OCULAR DEFECTS IN SURVIVING RAT EMBRYOS IRRADIATED ON TENTH DAY\*

Dosage	Total No. Embryos	Per Cent Anophthalmia	Per Cent Malformed	Per Cent Microphthalmia	Per Cent Unaffected
50 r	18	0.0	0.0	11.1†	88.9
100 r	40	2.5	15.0	57.5	25.0
200 r	31	29.0	29.0	35.5	6.5

\* Wilson & Karr (70).

† Slight.

TABLE III

OCULAR DEFECTS IN SURVIVING RAT EMBRYOS IRRADIATED ON NINTH DAY\*

	Number of Embryos Studied†	Per Cent Anoph- thalmic	Per Cent Malformed	Per Cent Microph- thalmic	Per Cent Unaffected
25 r	17	0	0	6	94
50 r	32	6	28	38	28
100 r	61	41	30	19	10
200 r	8	75	25	0	0

\* Wilson, Jordan &amp; Brent (72, 73).

† Only embryos removed 2 to 8 days after irradiation are included.

x-irradiation on the ninth day which caused *situs inversus totalis* and reversed tail with respect to sidedness. Wilson & Karr (70) exteriorized the contents of one uterine horn and irradiated the fetuses to doses ranging from 50 to 400 r. From 1 to 5 days thereafter fetuses were removed and studied for abnormalities. They found (a) a general retardation of growth resulting in proportionate smallness (b) localized retardation of growth with respect to the eyes, brain, aortic arches, lung, liver, and urinary organs (c) aberrant growth or malformations in eyes, brain, urinary organs and feet and (d) embryonic death with an exposure of 400 r which killed all fetuses within 24 hr. With regard to x-ray dose levels and the production of abnormalities, they found that at 10 days of gestation of the rat 50 r was totally ineffective; 50 to 100 r mildly effective; 100 to 200 r severely effective; and 200 to 400 r lethal. A dose of 100 r on the tenth day produced eye abnormalities such as anophthalmia or microphthalmia, in 75 per cent of the fetuses. An exposure of 200 r caused reduction in hematopoietic activity of the liver within 3 days of exposure.

In another study Wilson & Karr (69, 70) found that irradiation of fetuses on the ninth day by 200 r was lethal to all embryos but it took 400 r to kill all embryos 24 hr. later, on the tenth day of gestation. Abnormalities were produced by irradiation on either the ninth or tenth days but to produce defects comparable to those produced by 50 r on the ninth day it took 200 r on the tenth day. In either case, the eye was the most frequent site of maldevelopment.

After the exposure of the 9-day fetus, Brent & Jordan (8) found abnormal growths of compact masses of nervous-like epitheloid cells in the mesenchyme surrounding the brain at birth. In later papers Wilson (68) described these as neoplastic growths. These growths varied between some which grew and receded, others which remained compact and static, and still others which grew rapidly and killed the embryo. The growth of a specific mass



TABLE IV

MALFORMATION AND DEVELOPMENTAL RETARDATION OF SPECIFIC ORGANS OTHER THAN THE EYE IN SURVIVING RAT EMBRYOS IRRADIATED ON TENTH DAY\*

Dosage and Postirrad. interval Days	No. of Embryos Studied	Percentage of Embryos Showing Specific Defects		
		Malformations	Retarded Development	Liver Damage
100 r				
1	4	None	brain-100, urinary-75	0
2	9	brain-11	aortic arch-22, brain-11, heart-11	0
3	12	urinary-8	urinary-33, heart-25, brain-17, lung-17, aortic arch-8	8
4	7	urinary-29	heart-43, urinary-43, brain-29, aortic arch-29, lung-14	29
5	8	urinary-25	heart-87, urinary-63, brain-25, aortic arch-25	12
200 r				
1	4	brain-25	brain-75, urinary-75, lung-50, aortic arch-25	0
2	11	urinary-18, brain-9	aortic arch-64, brain-55, heart-55, urinary-46, lung-36	0
3	8	brain-25, aortic arch-25, tail-25, urinary-12, feet-25 (?)	brain-50, lungs-37, urinary-12	63
4	7	feet-86, brain-29, aortic arch-14	urinary-100, brain-43, heart-43, lungs-43, aortic arch-29	100
5	1	feet	general	yes

\* Wilson &amp; Karr (70).

seemed to be related to its blood supply. There was a direct increase in the incidence of these growths from exposures of 25 to 200 r. In 1952 Wilson, Brent & Jordan (71) further analyzed these neoplastic "tumor-like" growths which occurred in and around the brain and found that they never appeared before 24 hr. following irradiation of the 9-day fetus, and grew for varying lengths of time but all regressed before term. Those that remained at birth showed no evidence of proliferative growth and death could not be attributed to their presence. The tumors appeared to be nonmalignant and

TABLE V

RELATIVE INCIDENCE OF TUMORS IN VARIOUS LOCATIONS IN  
AND ABOUT THE BRAIN\*†

Postirr. Interval (Days)	Number of Embryos Studied	Incidence of Each Type as Per Cent of Total Growths				
		Polyploid	Rosette	Attached	Isolated	Cutaneous
2	13	8	0	37	38	17
4	18	2	1	19	57	21
6	22	6	14	20	56	4
8	8	6	18	29	47	0

\* Wilson, Brent, & Jordan (71).

† Based on animals receiving 100 r. Nine day rat embryos.

were derived from central nervous system primordia. The question was raised as to whether these regressed tumors might lie dormant and at some subsequent age of the rat resume the embryonic type of rapid growth.

Another paper (73) deals with a further study of the exposure of the 9-day fetal rat when the germ layers are laid down but there has as yet been no organ formation (differentiation). It was found that as little as 25 r caused microphthalmia in a few cases, 50 r retraded development and produced microphthalmia in 34 per cent of the fetuses, with certain brain and spinal cord abnormalities common. Exposure to 100 r caused ocular abnormalities in 90 per cent of the fetuses, increased mortality, and the survivors showed brain, spinal cord, face, heart, and circulatory disturbances. Exposure to 200 r killed all within 4 days, some within 24 hr. The overall effects were decidedly more severe than the same exposure given on the tenth day

TABLE VI

REDUCTION IN THE NUMBER OF TUMORS AS THE POSTIRRADIATION  
INTERVAL INCREASED\*†

	2	3	4	5	6	7	8	12 (term)
No. of Animals Studied	13	3	18	4	22	12	8	5
Per Cent of Animals Affected	92	100	100	100	100	52	88	40
Average No. Tumors per Affected Animal	4.0	16.0	7.8	7.0	6.6	4.3	4.2	2.5

\* Wilson, Brent & Jordan (71).

† Based on animals receiving 100 r.

of gestation "owing to the greater susceptibility of the less-differentiated ninth day embryo to mitotic delay and genic alterations."

In another paper (72) these authors state that exposure on the eighth day of gestation caused no maldevelopment except some retardation of growth up to 100 r.

"This difference in reactivity appears to be dependent upon whether cellular differentiation within the embryos has begun at the time of irradiation"

and

"The observations presented here warrant the conclusion that the pattern of response to irradiation in embryonic rats undergoes a qualitative change when cellular differentiation begins within the embryo."

Russell (49) drew the same conclusions for the mouse.

Hicks, in a series of 7 papers (23 to 29), some of which are currently "in press," has found in the rat embryo the same hypersensitivity of the neuroblast that had been described for the frog (42) and the chick (56) embryos. He believes that the neuroblast is as sensitive as is the hematopoietic elements in the embryo or fetus, because it is an actively differentiating cell. He distinguishes between the primitive germinal epithelium or neuroectoderm, the neuroblast, the immature, and finally the mature neuron. The neuroblast, he believes, is dynamically involved in the production of nucleic acids, sulfhydryl enzymes, and proteins necessary in differentiating growth which transforms it into an immature neuron. It is particularly sensitive to agents which inhibit sulfhydryl enzymes, to steroids, to cortisone, to aminopterin, and to radiomimetic drugs such as triethylene malamine (TEM), and to nitrogen mustard. In contrast the previous stage, the neuroectoderm, is resistant to radiation, to sulfhydryl agents, and to long periods of anoxia and hypoglycemia, as well as to direct ionizing radiations. It was therefore consistent to find that the neuroblast of the rat is also hypersensitive to ionizing radiations.

In studying the mouse and rat embryo Hicks found that x-ray exposure during the first eight days caused little demonstrable damage. Even when the exposure was as high as 400 r some of the litters survived. During this period there are no organ primordia. It is true that the composite cells of the embryo are multiplying but they are relatively radioresistant, probably because they are not in the process of differentiation. By the ninth day of gestation the situation becomes radically different with respect to radiation sensitivity. Gross malformations, particularly of the head region, followed even the low exposure of 30 to 40 roentgens which destroyed cells of the anterior striatum and its junction with the ventricular region. This is simply because the developing central nervous system at the anterior end, the potential primary brain, begins active differentiation of its neuroblasts toward immature neurons at this time. Likewise, the adnexa, the head mesenchyme, and the skeletal parts become active in the process of differentiation so that

x-irradiation causes brain, head, eye, and head skin anomalies. These are collectively classified as anencephaly. Only minor effects are manifest in regions posterior to the head.

By irradiation of the fetus on the tenth day there followed somewhat better development of the brain and the face, but the eye was still malformed. In many cases the nervous part of the eye was absent and only an abortive lens and lid formed. At birth there appeared some skeletal and visceral abnormalities not seen following earlier x-irradiation of the rat embryo.

## DEVELOPMENT OF THE RAT

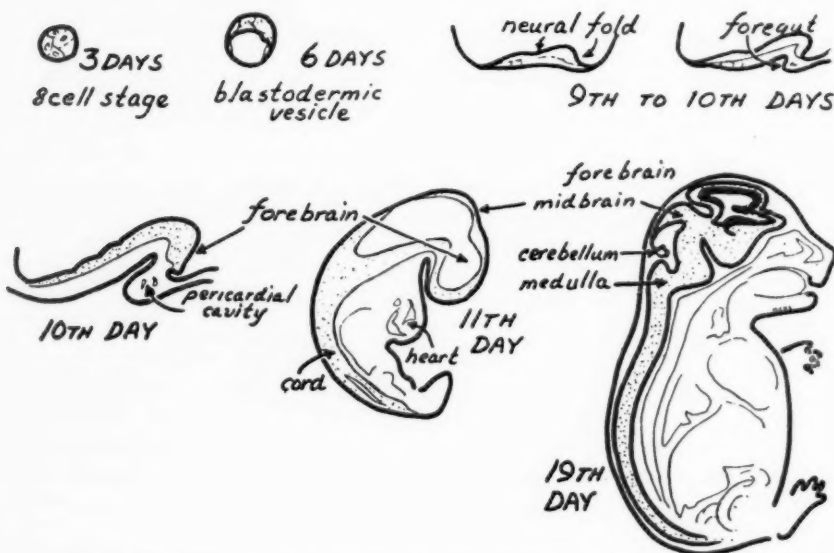


FIG. 3. Composite sketch of rat embryology showing active development of the neural folds and forebrain between 9th and 10th days. See Figure 5 for anencephaly produced by x-irradiation at this time. [Courtesy Hicks (27)]

Following irradiation on the eleventh day there was still better or more normal development of the brain, except for a narrow aqueduct. The major effects may be stated as hydrocephalus and encephalocoele. The retina was malformed, but the optic nerves appeared to be quite normal. Irradiation on the twelfth day had little effect on the development of the forebrain. Damage was seen in the hippocampus and the striatum, but more significant was the earliest evidence of cerebellar effects. These radiosensitivities in the cerebellum were destined to increase and persist for many days and even weeks after the time of birth because of the extended presence of neuroblasts.

TABLE VII

TIMETABLE OF RADIATION MALFORMATIONS IN THE RAT AND MOUSE\*

Time of Radiation	Brain Deformity	Other Malformations
First 8 days of Radiation	None	None
Ninth day	Anencephaly	None
Tenth day	Encephalocele and cerebral deformities	Skeleton, viscera, eye
Eleventh day	Narrow aqueduct, hydrocephalus, encephalocele	Skeleton, retina
Twelfth day	Porencephaly, cerebral defects, encephalocele	Skeleton, retina
Thirteenth to Twenty-first days	Decreasing degrees of microcephaly. Deformities of basal ganglia, cortex, hippocampus and corpus callosum	Decreasing skeletal and retinal malformations.
Sixteenth day to newborn period	Increasing cerebellar deformities	Stunted growth

\* Hicks (24).

A general survey of the rat radiation sensitivity shows that for eight days it is highly radioresistant; from the ninth to the twelfth day the development of its anterior structures is drastically affected by even low exposures to x-rays and such embryos as do survive are often destroyed by the mother at birth; and that irradiation after the twelfth day has little effect except at high doses which do cause some microcephaly, architectural disturbances in the cerebral cortex, the hippocampus, basal ganglia and cerebellum. There was some disfigurement of the striatum and corpus callosum and, following high doses, no corpus developed at all. As term was approached the skeletal malformations became less and less apparent, the retina and spinal cord became less radiosensitive, but the neuroblasts in the cerebellum and the striatum continued to make these regions highly radiosensitive. Prenatal irradiation disturbed the basic shape of the cerebellum but postnatal exposure altered its intrinsic cellular architecture, especially the granular cell layer. Irradiation on the ninth day produced a lobulated brain mass consisting of irregularly disposed neurons, nerve fibers (sometimes in bundles) and glia cells, and the anterior pituitary generally failed to make contact with the brain.

With specific regard to neuroblast sensitivity, when the concentrated neuroblast zones were exposed to as little as 150 r x-rays, many of the cells died but some continued to divide without apparent injury. The necrotic cells were quickly phagocytized. Within 24 to 48 hr. following irradiation the

residual or undamaged neuroblasts and the apparently normal neuroectoderm continued to proliferate and often formed rosettes and aggregations resembling primitive neural canals. These sometimes caused bizarre architectural patterns in and around the brain. Similar pinched-off potential neural cells formed in relation to the developing retina, causing deficiencies and malformation in that structure. These disconnected growths are probably the same structures as those described by Wilson (68) as neoplasms. However, Hicks (27), speaking of the possible offshoots of the neural parts of the optic vesicles and the anterior pituitary, states:

"It formed a mass of epithelial glandular elements, histologically reminiscent of oral mucous membrane appendages or even the cellular pattern of a craniopharyngioma"

and

"None of these tissues had the characteristics of true neoplasms, as has sometimes been implied."

Further, he states

"the growths here are simply the result of removing, or changing the growth rates of some of the developing building blocks in a normal embryo. In no instance did these

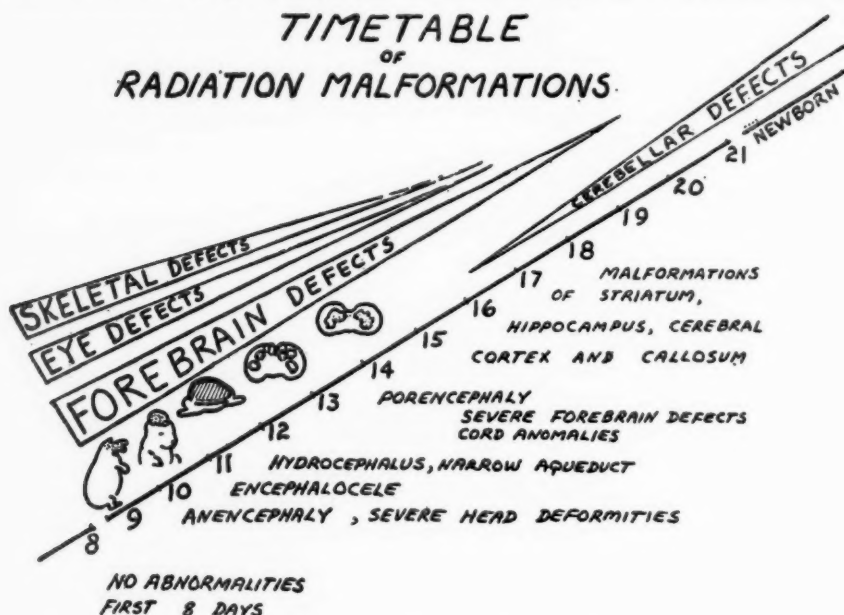


FIG. 4. X-irradiation of the rat embryo, showing major effects when irradiation insult is imposed at various intervals from 9 to 21 days of gestation. [Courtesy Hicks (27)]



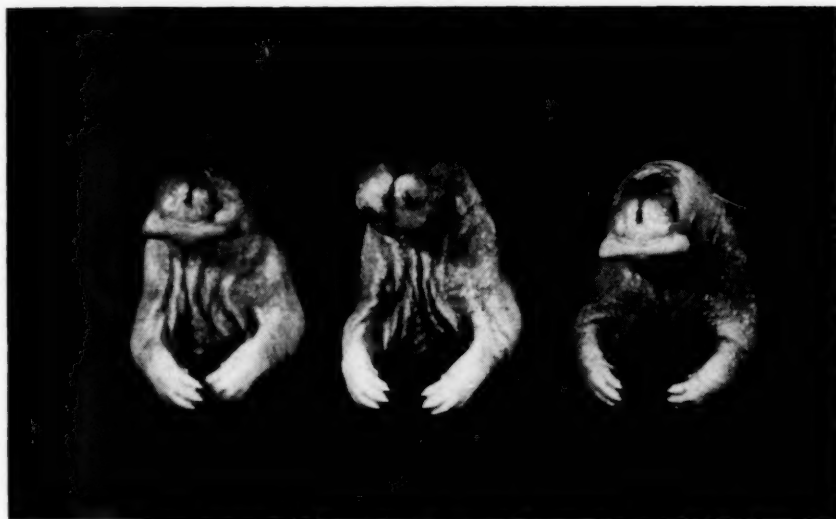


FIG. 5. Anencephaly at birth in rats which had been x-irradiated with 150 r on the 9th day of gestation. [Courtesy Hicks (27)]

abnormally formed tissues take on progressive and independent growth properties to the extent that they replaced, destroyed, or invaded other components,"

and

"To extend the term neoplasia to embrace every sort of abnormal growth would cloud an already very difficult concept."

It should be mentioned that Hicks was well aware of the possibility that radiation effects might be mediated through damage to the maternal tissues. He states, however, that placental damage was not achieved until an exposure of 400 r was used. This dose is much higher than necessary to damage the neuroblasts. He thus believes the effects on the embryo are direct. Also, he finds no parallel in sensitivity with mitotic activity, for in many instances the damaged neuroblast is not in the process of dividing. Further, mitoses were found in the radioresistant neuroectoderm as soon as 4 hr. following exposure to x-rays.

In summary, Hicks has shifted the emphasis in the fetus, not to a particular stage in development, but to the neuroblast as the most sensitive element, pointing out that at 9 days it is most abundant of all cells and therefore exposure on that day brings about gross nervous system abnormalities. The neuroblast is present, however, at other times and the cerebellum remains radiosensitive for some time after birth because it contains undifferentiated neurons. Hicks goes so far as to say: "Irradiation in successive stages

of pregnancy in rats produces a definite sequence of deformities, whose character is determined by what parts are in the neuroblast stage at the time of injury." Nevertheless, he is cautious about drawing any parallel with the radiosensitivity of the human fetus although he does say that the 9-day rat embryo is similar to the 16-day human embryo, but that the next few days of the rat are more like the fifth and sixth week of the human.

Accurate information relative to the exposure of the human fetus to specific doses of ionizing radiations is not at all abundant. One report may be cited. Hobbs (30) described the fetus exposed to 900 r at mid-pelvic depth at 5 months of age, which was delivered by Caesarian section and at 16 months post partum appeared to be quite normal. Of course, by 5 months the human fetus has achieved most of its active differentiation and is a functional being to the extent that it can survive premature delivery. On the basis of Hicks' studies with the rat one might suspect that there may yet appear certain cerebellar defects, and based on the studies of Rugh (46) there may well be some, if not complete, evidence of sterility.

#### DISCUSSION

There is no doubt but that either the embryo or the fetus as a whole is more radiosensitive than is the adult stage into which it develops. Such a statement does not reveal any of the underlying reasons for this hypersensitivity and it implies that the embryo is a homogeneous unit. Some of the reasons most frequently advanced are; (a) the embryo is metabolically the most active period in ontogeny; (b) there is always a higher mitotic index in the constituent tissues of the embryo than in the comparable tissues of the adult; and (c) the cells of the embryo are not only undergoing mitotic division but they are being transformed into the normal variety of tissues by a process of morphological and physiological differentiation. It is differentiation rather than mitosis that is radiobiologically so important in the embryo. The embryo is not a homogeneous unit but a mosaic of dynamically integrated regions, evolving toward a unified whole. Interference with the process of differentiation in any region of the embryo upsets the integration of development so that the effects are exaggerated and may involve other, but related, regions. The final organism at birth may, as a result, exhibit malformations.

Even before the appearance of formed organs the embryo is a mosaic of centers of highly integrated activity, both metabolically and by virtue of the process of differentiation. These centers must progress cooperatively, with respect to time and structure, toward a unified organism. Ionizing radiations are nonselective and ionized molecules are present equally in all regions of a totally exposed embryo. Obviously, either the inert primordium or the totally differentiated cell will be relatively radioresistant in terms of morphological change. The actively differentiating intermediate stage or stages will be highly radiosensitive since they are in the process of transformation

(differentiation). Thus, while the ionizing radiations are nonselective, the mosaic of presumptive tissues in various states of differentiation in the embryo will present a mosaic of reactants indicating different sensitivities. If the radiation is sufficient to insult a vitally important organ system during its formation, naturally the resultant organism will be malformed to a degree somewhat relative to the insult. In most embryological studies the criterion or measure of radiosensitivity is the extent of malformation at birth. However, it must be pointed out here that any specific insult at a critical moment whether by nitrogen mustards, anti-SH compounds, or by ionizing radiations, may bring about the same types of abnormalities. While ionizing radiations have many specific peculiarities, the embryonic responses are not new or peculiar. Ionizing radiations are a non-selective means of insult.

For the above reasons, the nonspecific but penetrating ionizing radiations, even at low levels, have provided us with valuable information relative to the time of initiation of development of specific organ systems. Russell indirectly pointed this out by admitting that ultimate malformations cannot always be attributed to irradiation of observable primordia "because certain sensitivities appear before their primordia." The initial steps in differentiation may well occur before they can be perceived. Similar malformations are never produced by irradiation of the formed organ. Radiation damage is instantaneous, or immediate, but the manifestation of it is delayed. Nevertheless, on the basis of these facts we now have a more accurate schedule or pattern of development of organ primordia. An exposure of 300 r x-rays of the rat fetus on the ninth day will invariably produce defects in the central nervous system, particularly in the brain, because at the time of irradiation presumptive brain is in the neuroblast stage, and this stage of neuron formation is demonstrably radiosensitive.

With regard to the extraneural aggregations of cells sometimes referred to as "tumor-like" or "neoplasias" it is the belief of this reviewer that x-irradiation at any stage, critical for certain cells, may provide such separation of cellular aggregates. It is unwise to use the word tumor which is defined by Willis (65) as follows: "A tumor is an abnormal mass of tissue, the growth of which exceeds and is uncoordinated with that of the normal tissue, and persists in the same excessive manner after cessation of the stimuli which evoked the change." None of these excrescences from the developing central nervous system or retina fit the definition of a tumor.

The adult vertebrate organism is made up of the usual tissues which can be graded as to radiosensitivity. This same scaling cannot be applied to the tissues of the developing organism. Neither can the embryo be considered as functioning as a single tissue because: (a) the production of abnormalities or lethality in the embryo will vary greatly from day to day during embryonic life and; (b) its radiosensitivity is based on the sensitivity of its most actively differentiating cells at the time of irradiation. There is nothing peculiar to embryonic radiosensitivity when we remember that every embryo contains

more differentiating cells than does the adult into which it develops. It is the presence of the differentiating rather than the dividing cell that gives to the embryo and to the fetus its particular radiosensibilities.

One cannot ignore the all-important but scattered references to the x-irradiation of the human fetus. The criticisms which apply to the earlier works in radioembryology apply now to the papers on the human fetus, largely because the material is obtained incidentally or accidentally. The most recent paper [Hobbs (30)] reports the x-ray exposure of a human fetus at 19 to 20 weeks to 900 r mid-pelvic level with subsequent Caeserean delivery. The child was examined at 16 months of age and did not show any detectable signs of radiation damage.

Two aspects of these data should be emphasized: (a) The fetal age was far beyond that as a result of which immediate irradiation damage would be expected, for the fetus was histologically rather fully differentiated except, possibly, for the eyes, cerebellum, and gonads. (b) The dose was such that if the individual never exhibits sterility, cataracts, blood dyscrasias, lowered resistance to disease, or shortening of life span, it would be very significant. The accepted tolerance level for that fetal age would then have to be reconsidered.

One cannot draw conclusions from an isolated case such as this, even though the radiation dosimetry and fetal age were accurately determined, Contrariwise, even if this case proves to be sterile one cannot attribute this sterility solely to an x-irradiation cause. Such a conclusion might be circumstantially derived in about 80 per cent of all males since that is roughly the level of normal fertility. With the active cooperation of research-minded gynecologists and obstetricians the radioembryologists will eventually accumulate enough data so that the problem can be evaluated properly with respect to the x-irradiation hazards to the human embryo and fetus.

#### SUMMARY AND CONCLUSIONS<sup>\*</sup>

1. Poikilothermic embryos such as those of the fish and amphibia exhibit slow responses following exposure to ionizing radiations. This is probably attributed to the low environmental temperatures characteristic for these forms.

2. The kinetic mechanism for cleavage may be unaffected by x-irradiation even to a level which will neutralize all of the chromosomes in either gamete.

3. Egg nuclei may be damaged directly. There is also some evidence that they may be damaged indirectly by exposure to previously irradiated egg cytoplasm.

4. There is no evidence of recovery of embryonic cells from the effects of ionizing radiations. Recovery is defined as a return to the pre-irradiated state by the cell.

<sup>\*</sup> Based on the works reviewed in this chapter.

5. Destruction which follows x-irradiation, such as pycnosis, may be delayed by low temperatures or anoxia but it will occur in due time or upon restoration of the normal conditions of temperature or oxygen tension.

6. The newly fertilized egg is more radiosensitive than is either gamete, as measured, not by survival, but by the effects on embryonic development.

7. X-irradiation at various stages of development elicits different malformations at hatching or birth and it is possible to obtain a high incidence of a specific abnormality by irradiation of the embryo at a specific time. The organ primordium most actively differentiating (not merely multiplying its cells) at the time of the radiation insult, will prove to be the most radio-sensitive. The organ system into which this organ primordium eventually develops will exhibit the maximum malformation, and may even cause embryonic death.

8. In early embryos the neuroblast is among the most radiosensitive of cells and is comparable to the hematopoietic primordial cells of the adult. Since they are present in the cerebellum of mammals for several weeks after birth, the brain remains especially sensitive to ionizing radiations.

9. Killing of embryos is attributable not to over-all radiosensitivity, but to that of specific cell types or organ primordia. There is a wide range of tolerance of formed organs of the adult, but probably a lesser variation in the tolerance among the embryonic organ primordia.

10. Some organs, which would succumb in an irradiated embryo, will survive if transplanted to an unirradiated host. This fact further supports the thesis that embryonic lethality may be merely an indication of a specific vital organ primordium sensitivity.

11. Regeneration from a larval blastema may be affected by x-irradiation in a manner similar to irradiation of the original primordium, and is related to the effect on mitosis and on differentiation.

12. Irradiation of the mouse embryo during the preimplantation stage reduces the litter size suggesting that the effect may be indirectly by way of the maternal tissues, preventing implantation, as well as directly upon the embryo.

13. Radioresistance during the first eight days of mammalian (mouse and rat) embryonic life is attributed to the absence of differentiation rather than to the lack of placental relations. There is maximum sensitivity from 9 to 16 days, with the peak at 9 days, when there is an abundance of differentiating neuroblasts. After the sixteenth day fetal response is quite similar to that of the adult.

14. Extraneural lesions of the brain are produced in most of the offspring of rats exposed to 100 r on the ninth day, but they are usually resorbed by birth. There is no conclusive evidence that these lesions are permanent or malignant in any way. Similar retinal lesions appear to be more permanent.

15. Growth may be retarded at levels of exposure too low to produce gross abnormalities. Such exposures also may produce delayed effects such as

shortening of life, cataracts, skin defects, tumors of old age, and lowered resistance to disease.

16. Since 40 r x-rays will damage some mammalian neuroblasts at the time of their differentiation, this dose might be taken as suggestive for consideration for a maximum level in clinical practice where pregnancies are involved. Nevertheless, it must be restated that conclusions from a study of the mouse and rat embryonic radiosensitivities cannot be interpolated for the human fetus, they can be only suggestive. The suggestion is obvious, namely, that radiological examinations of the human female be restricted to the ten days following menstruation to avoid any possibility of embryonic or fetal exposure.

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## VERTEBRATE RADIOBIOLOGY: HISTOPATHOLOGY AND CARCINOGENESIS<sup>1,2</sup>

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Knowledge of the histopathologic and carcinogenic effects of ionizing radiation has been amplified greatly under the impetus of atomic fission. Recent research has yielded significant contributions on relationships between dose, dose rate, type of radiation (electromagnetic and particulate), and biologic effectiveness; on synergistic and antagonistic factors modifying the biologic effectiveness of radiation; on radiation protection; on the mechanisms of direct and indirect effects resulting in acute and delayed radiation injury, notably hemorrhage, microbic invasion, leukemia, neoplasia, and cataract; and on species and strain differences in radiosensitivity. The older literature is reviewed by Lacassagne (1, 2, 3) and Warren *et al.* (4, 5). Bloom (6) describes in detail the histologic studies of the Plutonium Project, and Hempelmann *et al.* (7, 8) survey radiation effects in man. Relevant references are included in recent reviews by Brues (9), Cronkite & Brecher (10), Curtis (11), and Patt (12), and the carcinogenic action of radiations has been discussed in historical perspective by Furth & Lorenz (13).

It is accepted that particulate irradiation produces essentially the same changes as electromagnetic irradiation; both act ultimately by causing ionizations and may be compared quantitatively by expressing ionization values in terms of "rep" and "rem" [Evans (14)]. In general, adult and resting cells are radioresistant, while mitotic or metabolically active cells are sensitive; thus, susceptibility to acute injury is a function of cellular replacement or growth. Liability to tumor-induction, on the contrary, is not dependent on mitotic activity alone; e.g., the replacement rate of epithelial cells of the cornea and small intestine is high, yet they do not give rise to tumors. It seems that both direct and indirect mechanisms are at play in determining the magnitude and character of radiation damage, particularly with respect to induction of neoplasia, but knowledge of these mechanisms is still scant.

### GENERAL

*Cytologic effects.*—The alterations in nuclei and chromosomes caused by

<sup>1</sup> The survey of the literature pertaining to this review was concluded in February, 1953.

<sup>2</sup> The following abbreviations are used: DNA for deoxyribonucleic acid; RNA for ribonucleic acid; ATP for adenosinetriphosphate; TSH thyroid-stimulating hormones.

<sup>3</sup> Work performed under Contract No. W-7405-eng-26 for the Atomic Energy Commission.

x-rays, fast neutrons, and  $P^{32}$  are qualitatively indistinguishable [Warren *et al.* (15, 16)]. Radiosensitive cells develop prominent intranuclear vacuoles which cause lethal rupture of nuclear membranes, while radioresistant cells form smaller intranuclear vacuoles that are extruded. The Feulgen stain shows a loss of DNA<sup>2</sup> proportional to radiosensitivity. In the irradiated liver abnormally large amounts of pyronin-positive material, believed to represent ribose nucleic acid, collect around the nuclear membrane. These observations suggest a relationship between loss of nuclear DNA and gain of RNA in the cytoplasm. Radiomimetic substances (aminopterin, urethan, and nitrogen mustard) and colchicine induce cytologic and histochemical changes similar to those of irradiation (15, 16). However, in rats after equally damaging doses of nitrogen mustard ( $HN_2$ ) and of x-rays (200 r  $\approx$  1 mg.  $HN_2$ /kg.), the following differences were noted: After 200 r, chromosomal injuries decreased in 12 hr. and were absent in 75 hr., while after  $HN_2$  the proportion of injured cells increased with time, reaching 90 per cent in 144 hr.; cells were most sensitive to x-rays at the beginning of prophase but to  $HN_2$  mainly in the intermitotic phase; systemic effects were greater with  $HN_2$ . Thus, the similarity between these two agents is merely that of end-results, and the term "radiomimetic" is misleading [Koller & Casarini (17)].

Following 700 r cells<sup>4</sup> of the crypts of the small intestine, the most radiosensitive elements of the gut, revealed a decrease and later an increase of stainable DNA, cytoplasmic and nuclear RNA,<sup>2</sup> and nucleolar alkaline phosphatase. By the sixth day there was marked increase in DNA and RNA, with reduction of alkaline phosphatase, and numerous mitoses. The alkaline phosphatase in the nucleus appeared to be related to the turnover of phosphorus of DNA [Tillotson *et al.* (18)]. Diminution of histochemically demonstrable nucleic acid in irradiated cells was confirmed. Radiosensitivity was found to be greatest when the thymonucleic/ribonucleic acid ratio was highest [Cornil & Stahl (19)].

Continuous local irradiation of the epithelium of the tongue with doses of  $P^{32}$  that produced minimal necrosis resulted in formation of large atypical nuclei containing masses of chromatin. Treatment of sections with desoxyribonuclease markedly diminished the stainability of irradiated as contrasted with normal nuclei, suggesting that continuous irradiation resulted in depolymerization of nucleic acid complexes [Burstone (20)].

Organs poor in acetal-phosphatids were particularly radiosensitive, and those rich in this substance were radioresistant, suggesting that acetal phosphatids were important in the resistance or regeneration of tissues [Hornykiewytch *et al.* (21)]. Knowlton & Widner (22) found that differences in the mitotic indices of various tissues were primarily attributable to variations in intermitotic times. Sensitivity to x-rays varied inversely as the intermitotic time in the seven tissues studied, the decreasing order of sensitivity being: jejunum, nucleated red blood cells, myelocytes, ovarian follicles,

<sup>4</sup> Unless noted otherwise total-body x-irradiation is implied by r.

lymph node, epidermis, and adrenal cortex. Exposure to 50 r depressed mitotic activity within 30 min. in all of these tissues.

**Differentiation.**—Penetrating radiations can change the type, extent, or degree of cellular differentiation [Glucksmann (23)]. In the squamous epithelium of the uterine cervix 2000 to 4000 r may cause an increase in the rate of differentiation; in the ducts and acini of mucous glands the reserve cells form a squamous epithelium which gradually replaces the normal columnar epithelium. Likewise, mucin-producing cells of the bronchus react with squamous metaplasia. Chromosomal injury, while allowing cells to differentiate, prevents them from undergoing division (23).

**Protection.**—There was a marked erythroblastic metaplasia in the lead-shielded spleen of the irradiated mouse and a hastened recovery of the gastrointestinal tract, lymphoid tissues, and bone marrow, though not of the testis and ovary. In rabbits the erythropoietic metaplasia of the shielded spleen was not seen, and recovery was not as markedly enhanced [Jacobson *et al.* (24)]. No histologic evidence of increased regeneration of bone marrow or of ectopic hemopoiesis was found to account for the increased survival afforded by shielding small amounts of ectopic bone marrow, induced in the tails of rats by abdominal implantation [Storer *et al.* (25)]; however, in experiments of Kaplan & Brown (26), shielding of the thigh accelerated recovery of the thymus and hemopoietic tissues in x-irradiated mice. Congdon *et al.* (27) observed that transfusions of bone marrow did not detectably alter the radiation-induced damage of the hematopoietic system of guinea pigs and mice but greatly accelerated recovery, thereby enabling survival. The fate of intravenously-injected bone marrow cells was unknown. Intraperitoneally-injected marrow became necrotic and was later organized and ossified. Heterologous marrow was less protective than homologous marrow. These observations favor the humoral theory of protection (27). Edwards & Sommers (28) found no radiation damage in the shielded partner of irradiated parabionts such as might be produced by circulating substances; the leukocytes of the shielded rat appeared to bolster the irradiated partner. Cysteine did not reduce the chromosomal injury in cells of the bone marrow, as did hypoxia; it is inferred that protection by the former is exerted in the cytoplasmic enzyme systems and by the latter in the chromosomes [Devik (29)]. The late effects in rats exposed to 600 to 1400 r under anoxia were: marked shortening of life span; a high death rate attributable to pneumonia; nephrosclerosis and generalized arteriosclerosis; hypertension; and thrombocytopenia and anemia, suggesting hypersplenism. In animals with early changes splenectomy was followed by a marked rise in platelet levels. There was cachexia and late epilation over the head and neck. No leukemias or tumors, other than fibroadenomas of the breast, were encountered [Bennett *et al.* (30)]. In the hibernating marmot lethal radiation resulted in the usual pattern of injury only in tissues undergoing cell division (testis and ovary); injury to other organs, such as the hemopoietic system, was delayed until resumption of the nonhibernating state [Brace (31)]. Other aspects of radiation protection have been reviewed by Patt and Brues (32, 33).

*Acquired radioresistance.*—In the duodenal epithelium of the mouse exposed daily to 60 r, there was a decrease in debris and persistence of mitoses when the total dose had accumulated to 2100 r. The number of mitoses never exceeded that of the untreated controls [Bloom (34)].

*Carcinogenesis.*—Tumor induction by ionizing irradiation can be brought about: (a) by direct action (e.g., in skin, bone, and hemopoietic tissues); (b) cocarcinogenic effect (inflammation, aseptic or microbial, fractures, carcinogenic hydrocarbons); and (c) indirect action (known only in animals; includes lung, ovarian and mammary tumors, and leukemias) [Glücksman (35)].

*Chronic exposure.*—Lorenz (36) has studied the effects of daily doses of 0.11 r to 8.8 r (given in 8 hr. per day, 6 days weekly) on mature mice, guinea pigs, and rabbits, exposed for the duration of life. In general, the biologic effects decreased with the dose rate, presumably as a result of recovery between successive exposures. Survival decreased as a linear function of mean accumulated dose. In mice, carcinogenesis was more important in shortening the life span than in the other two species. The histologic effects of chronic irradiation of mice [Spargo *et al.* (37)] and of dogs [Metcalf & Inda (38)] are similar to those of acute exposures.

The pathologic changes in rats, rabbits, and dogs exposed to fast neutron radiation (cyclotron) at dosage levels of 0.012, 0.06, 0.11, and 1.7 n per day,<sup>5</sup> six days weekly for one year, were as follows: an increased incidence of infections in rats at the 1.7 n dose level (pulmonary and paratyphoid infections were most common), neoplasms, atrophy of hemopoietic tissues and gonads, and hemorrhage [Ely *et al.* (39)]. The biological effects of deuterons of high energy (190 Mev) are essentially the same as those of roentgen rays and protons. However, they enable a sharp delineation between irradiated and unirradiated tissues. If tumor contours are accurately known, regression of radiosensitive growth is readily achieved [Tobias *et al.* (40)]. Irradiation of various small parts of the rat with this deuteron beam ( $\frac{3}{8}$  or  $\frac{3}{4}$  inches in diameter) resulted in negligible acute mortality except after lateral exposures of the abdomen. Mortality was poorly correlated with dose over the range employed (864 to 5076 rep) [Swift *et al.* (41)]. The blood and tissue changes resulting from deuteron irradiation are proportional to equivalent doses of other types of ionizing radiations [Rosahn *et al.* (42)].

*Additivity.*—Dissimilar radiations from the thermal column of the Los Alamos Homogenous Reactor and from a 250 kv. x-ray machine were found to be completely additive and exhibited no synergistic or antagonistic action [Storer & Harris (43)].

*Atomic bomb exposure.*—The anatomic sequelae of atomic bomb radiation have been enumerated in several recent reports [Bruegge (44)], [Capretti (45)], [DeCoursey (46, 47)]. The lymphoid and hemopoietic tissues, skin,

<sup>5</sup> An n unit is that amount of fast neutron irradiation which produces a reading of one scale unit on a Victoreen condenser r-meter equipped with a 100-r chamber.



TABLE I  
IMPORTANT ANATOMIC CHANGES IN JAPANESE DYING OF ATOMIC BOMB IRRADIATION

Tissue	Patients dying in weeks 1 and 2	Patients dying in weeks 3 to 6	Patients dying after 6th week
Adipose tissue	Usually no emaciation	Occasionally emaciation	Usually emaciation
Lung	Occasional hemorrhage and edema	Necrosis and hemorrhage	Focal necrotising or organizing pneumonia
Bone marrow	Atrophy	Usually atrophic Occasionally marked reticulum hyperplasia Focal myeloid regeneration Marked myeloid hyperplasia	Usually focal myeloid regeneration Marked myeloid hyperplasia Occasionally atrophy, marked reticulum hyperplasia
Lymph nodes and spleen	Extreme decrease of small lymphocytes	Same. Atypical mononuclear cells	Same. Occasionally lymphoid regeneration
Liver	Giant nuclei, congestion and edema of central veins	Occasionally congestion Usually fatty degeneration	Frequently fatty degeneration and focal necrosis
Gastrointestinal tract	Atypical mitotic and resting epithelial cells	Necrosis, hemorrhage and ulceration	Necrosis and ulceration
Neck organs	Atypical mitotic and resting epithelial cells	Necrosis, hemorrhage and ulceration	Focal necrosis and ulceration
Skin	Unknown	Petechiae and necrosis Atrophy of hair follicles	Regeneration of hair follicles Usually no other changes
Gonads	Incipient atrophy	Severe atrophy	Extreme atrophy

Polymorphonuclear leukocytes were rare or absent in lesions of patients dying three to six weeks after exposure.

genital organs, and gastrointestinal tract were most severely affected by ionizing radiation. The principal histopathologic changes observed in Japanese victims in relation to time after exposure are summarized in Table I [Oughterson *et al.* (48)].

*Radioactive substances.*— $P^{32}$ , by virtue of its distribution, acts as a powerful hemopoietic poison, producing aplasia of the bone marrow and hypoplasia of all lymphoid tissues. In rats, the small bowel and the gonads are also sensitive; liver, pancreas, adrenals, kidney, heart, and brain are resistant. Destruction of tissue is evident from 6 to 12 hr. after injection of  $P^{32}$ . The late effects include osteogenic sarcoma and squamous cell carcinoma of the skin [Koletsky & Christie (49)]. Both the amount of  $P^{32}$  entering the tissues and their radiosensitivity determines the amount of radiation damage produced; thus, the destructive effects in rats are intense only in some of the tissues with a high  $P^{32}$  content (hemopoietic tissues, intestinal crypts, and ovarian follicles) and not in others (liver and kidney). In all organs and tissues with a low  $P^{32}$  content, including pancreas and nervous tissue, little or no destructive effect occurs [Grad *et al.* (50)]. The effects of  $P^{32}$  in mice are similar. In the small intestine no new cells are supplied from the crypts to balance the continual loss of cells by extrusion at the tips of the villi. Lesser changes are noted in the stomach and colon, and in hair follicles and testis and none in the salivary glands, pancreas, liver, urinary tract, endocrine organs (other than gonads), brain, muscle, and connective tissue. Thymic involution may be caused in part by adrenal stimulation [Grad & Stevens (51)]. These findings confirm those of Warren *et al.* (52, 53). Doses comparable to clinical doses in man (0.066 to 0.166  $\mu$ c. per 100 gm. of  $P^{32}$  or 0.2 to 6.00  $\mu$ c. per 100 gm. of  $I^{131}$ ) produce no histological changes detectable six weeks after administration in the liver, kidney, adrenal, or testes of rats weighing 100 gm. [Moses *et al.* (54)].

The physical and medical problems in relation to radium and mesothorium deposition in 30 persons have been thoroughly investigated by Aub *et al.* (55). The fundamental features of acute poisoning are severe anemia, attributable to marrow destruction, and "jaw disease" attributable to destruction of the alveolar crests with secondary infection. Chronic poisoning causes neoplasms in or near bones (55). Based on few observations in man and dog the following damage is attributed to radiothorium (RaTh): depression of hemopoiesis, cachexia, exacerbation of latent infections (as tuberculosis), and formation of malignant tumors, such as myeloma and osteosarcoma [Zadek (56)]. Polonium, plutonium, and radium produced changes in rats comparable to those resulting from whole-body x-radiation; however, in radium-injected rats calcification of tracheal cartilage and calcific arteriosclerosis also were encountered as delayed effects [Casarett *et al.* (57)]. Plutonium, and radium-injected rats showed a decrease in osteoblasts and osteoclasts, with degeneration and disorganization of the epiphyseal line of bone (57). In rats progressive nephrosclerosis followed the intravenous injection of 10  $\mu$ c./kg. of polonium, associated with generalized

arteriosclerosis, cardiac hypertrophy, and renal failure. These findings are similar to those reported by Bennett *et al.* (30) in heavily x-irradiated rats. The severe arteriosclerosis led to atrophy of the affected tissues and inhibited recovery from radiation injury [Casarett (58)].

#### HEMPOIESIS

Injury to lymphoid and erythropoietic tissues is evident in mice within the first hour after 625 to 1000 r (56, 60), and is severe after 14 hr. Regeneration usually begins within 100 hours [Lamson & Tullis (59)]. One week following 1500 r of 2 Mev x-rays ( $LD_{100}$ ) the bone marrow of hamsters was depleted to about 10 to 20 per cent of its original mass, the thymus to about 25 per cent, and lymph nodes and spleen much less. Phagocytosis was most evident in the lymph nodes. The most radiosensitive cells were lymphocytes, myelocytes, and erythrocyte precursors in that order. Reticulo-endothelial cells were radioresistant. When death occurred under the x-ray beam (110,000 r in  $3\frac{1}{2}$  hr.), the thymus and bone marrow had the greatest cellular reduction, and the lymph nodes were next. The spleen was considerably enlarged. All organs studied showed an immediate dispersion of lymphocytes and lymphopenia. Hemorrhage was most evident in the spleen and the bone marrow. Mitosis was stopped abruptly. Pyknosis and karyorrhexis were widespread. Nuclear and cytoplasmic swelling were more evident in the thymus and bone marrow than in the other organs studied. There was little change, if any, in the connective tissue [Rugh *et al.* (61)].

Lorenz (62) exposed guinea pigs to 8.8 r daily of  $\gamma$ -radiation for 110 days. The bone marrow of guinea pigs dying a few weeks after discontinuation of the irradiation was of normal cellularity, but megakaryocytes were nearly absent, even though the platelet levels had increased. In those in which abortive recovery took place, the bone marrow was markedly hyperplastic but without megakaryocytes; yet there was some recovery in platelet levels to about one-half normal, and granulocytopenia. This might be explained by the presence of extramedullary hemopoiesis in the spleen of the chronically exposed animals. Recovery of the hemopoietic system was more rapid after acute than after chronic exposure. After 2.2 r daily, or larger doses, the principal cause of death in guinea pigs, surviving 18 months or longer, was pancytopenia [Lorenz (36)].

In mice, median-lethal doses of  $P^{32}$  produced maximal injury of the thymus in two to five days, and affected the bone marrow later. Injury was greater at the ends of long bones than in the shaft, in keeping with the localization of  $P^{32}$  [Warren *et al.* (53)].

A marked increase of mast cells was observed in the hemopoietic organs of rats exposed to 2000 r. This was biphasic, the first wave of mast cells appearing within 3 to 24 hr. and the second within 60 to 70 hr. postirradiation. Mast cell increase occurs also after diabetogenic doses of alloxan [Arvy *et al.* (63)]. Increase in mast cells was noted in the thymus of the

hamster after 995–1200 r; this could not be produced by starvation, cortisone, or adrenal cortical extract [Kelsall & Cragg (64)].

**Bone marrow.**—Following 700 r, the erythroid cells of rats rapidly decrease in number and the myeloid cells undergo accelerated maturation. The rate of decrease in megakaryocytes, mast cells, and lymphocytes is related to their life spans, assuming absence of further production. The absolute number of reticulum cells and plasma cells is unchanged. Formation of new cells, except possibly of plasma cells, is completely inhibited for the first nine days. Regeneration is first evidenced at twelve days by areas of erythropoiesis and, to a lesser extent, myelopoiesis. Megakaryocytes reappear in small numbers at 15 days. Transition of reticulum cells to mast cells is observed [Rosenthal *et al.* (65)]. Injury is evident in rats within the first hour after 550 r. Red cell precursors degenerate earlier than the myeloid series but also regenerate earlier. Recovery occurs by the 40th day [Metcalf *et al.* (66)]. In swine, erythroblasts begin to show necrosis within 9 hr. after 600 r, and all are nearly gone by 13 hr. [Tullis (67)].

The bone marrow is destroyed in mice by  $P^{32} \sim 20 \mu\text{c./gm.}$  administered systemically. It is subsequently replaced by reticular cells which contain greater than normal amounts of glycoprotein, glycogen, and alkaline phosphatase, and are associated with a glycoprotein-containing matrix which calcifies. It is postulated that the glycoprotein matrix is in a state of sub-normal aggregation [Burstone (68)]. After intraperitoneal injection of  $P^{32}$ ,  $4.3 \mu\text{c./gm.}$ , into rats damage of myeloid elements is maximal at seven to nine days, when the first signs of recovery are also present. The marrow returns to normal within 60 days. No effect on erythroid tissue is detected [Phillips *et al.* (69)].

Intravenous injection of radiothorium results in depression of hemopoiesis [Zadek (56)]. The bone marrow of man injured by  $\text{ThO}_2$  exhibits general atrophy, with delay of maturation and marked hyperplasia of reticulum cells [Rotter (70)]. Severe anemia with marrow aplasia is a feature of radium and mesothorium poisoning only in those persons receiving large quantities of these substances who die soon after exposure. Review of human cases indicates individual variations in sensitivity [Aub *et al.* (55)]. Hypoplasia of the bone marrow has been observed also in patients treated with  $50 \mu\text{c.}$  or more of colloid gold (Au 198) [Botsford *et al.* (71)].

**Hemorrhagic tendency; anemia.**—Recent studies point to platelet deficiency as the major factor in the development of hemorrhage following massive irradiation of the whole body or the bone marrow. The reduction of megakaryocytes in rats between the fourth and twelfth days after 550 r is paralleled by a drop in the number of circulating platelets. Microscopic hemorrhage occurs often and anemia is most profound during this period [Metcalf *et al.* (66)]. The hemorrhagic tendency and anemia of irradiated dogs is characterized by thrombocytopenia. The clotting time is commonly prolonged, but prothrombin activity and conversion accelerators are not

significantly altered. An anticoagulant is present in the blood of some animals. The hemorrhage may be controlled with toluidine blue but not with frequent blood transfusions. Some alteration in capillary fragility unrelated to thrombocytopenia is assumed but not demonstrated [Allen *et al.* (72)]. Brecher & Cronkite (73) have shown that hemorrhage in the lymph nodes of dogs after 400 to 600 r is prevented by daily transfusions of platelets in sufficient numbers to maintain the levels at 100,000–200,000/mm.<sup>3</sup>. Cronkite *et al.* (74) interpret available data as indicating that ulcero-necrotic lesions and infections play a prominent role in initiating hemorrhage, purpura being frequently correlated with sepsis. While a deficiency of platelets is amply proven, that of other factors of blood coagulation remain to be demonstrated. Failure of prothrombin utilization is correlated with platelet deficiency (74). The early postirradiation anemia is intimately related to the hemorrhagic state [Bigelow *et al.* (75)], [Furth *et al.* (76)], [Ross *et al.* (77)], [Kahn *et al.* (78)]. For a few days following exposure to midlethal doses of x-rays the erythrocyte mass drops, attributable to failure of erythrocyte production and to death of over-aged erythrocytes. After the first week erythrocytes appear in the lymph, their number rapidly rising above 1,000,000/mm.<sup>3</sup> in fatally irradiated animals; most lymphatics at this stage are red at autopsy. However, clinical and anatomical manifestations of hemorrhage are preceded by diversion of erythrocytes into the lymph; thus, erythrocyte counts of the lymph are a fair index of the degree of endothelial fragility. Diversion of erythrocytes into extravascular spaces, lymphatics and lymph sinuses may cause loss from the blood stream of more than one-third of the erythrocyte mass (relative anemia). The extravasated erythrocytes are drained into the sinuses of lymph nodes, where they are engulfed by macrophages and the hemoglobin converted into hemosiderin. Histologic changes indicative of this sequence of events are noted in fatally irradiated animals of all species dying during the "hemorrhagic diathesis." That extravasation of erythrocytes is associated with their destruction is indicated by the massive erythrophagocytosis and hemosiderosis in spleen, lymph nodes, and bone marrow. Conditions prevailing in tissue spaces, notably in x-rayed hosts, alone may be injurious to erythrocytes; however, a hemotoxic effect of the lymph has not been shown experimentally. Hemotoxic substances may be liberated from injured cells or from bacteria. Erythrocyte destruction is attributable to irradiation not of erythrocytes but of the host (78), since normal erythrocytes labeled with Fe<sup>59</sup> are just as readily destroyed when introduced into an irradiated host as when both host and labeled erythrocytes are irradiated simultaneously.

Extending the demonstration of Brecher & Cronkite (73) that transfusion of platelets diminishes or prevents the hemorrhagic tendency, Woods *et al.* (79) have shown that after homologous platelet infusion the erythrocyte count in the lymph of massively irradiated dogs drops within 30 min. from above 1,000,000/mm.<sup>3</sup> to a few thousand, so that the bloody lymph becomes



clear again. These observations support the theory that the hemorrhage results from deficiency of platelets which are required to maintain the integrity of the endothelial membrane.

A chronic hemorrhagic state with aplastic anemia has long been known to exist following deposition of bone-seeking radioactive substances. In a man who died of  $\text{ThO}_2$  intoxication 10 years after arteriography there were heavy deposits of thorotrast in macrophages of spleen, lymph nodes, liver, and bone marrow. There was a hemorrhagic "diathesis" associated with necrotizing arteritis and diffuse hyperplasia of the bone marrow, resembling diffuse myeloma, with reduction of erythrogenic cells. The lymphoid tissues were atrophic. The picture was that of aplastic anemia with leukopenia and thrombocytopenia [Schmidt *et al.* (80)].

*Spleen and reticulo-endothelial system.*—Lymphoid atrophy in the spleen occurred in rats within the first hour after 550 r. Regeneration approximated normal by the 40th day [Metcalf *et al.* (66)]. Moderate lymphoid atrophy in the spleen, followed by regeneration to normal within 60 days occurred in rats after intraperitoneal injection of 50  $\mu\text{c.}$  of  $\text{P}^{32}$ . Myeloid elements were not detectably affected [Overend *et al.* (81)]. Fibrosis of the spleen and lymph nodes, with marked intralobular fibrosis of the liver, were noted in a woman who had received a large dose of  $\text{ThO}_2$  in an empyema cavity 15 years before. Granular thorotrast was demonstrated in tissues by radioautograms. The sclerosing effect was attributed to radioactivity as well as to mechanical and chemical irritation [Frangia & Costa (82)]. Intravenous injection of thorotrast, 1 to 3 ml./kg., into rats, led to cytologic changes in reticulo-endothelial cells in the liver, judged to be of a "precancerous hemangioendothelioma" type [Christensen & Sommers (83)].

The function of phagocytosis by reticulo-endothelial cells of x-rayed rabbits was assayed by determining the rapidity of removal of intravenously injected colloidal gold. At no time following x-radiation up to  $\text{LD}_{50}$  doses was the gold colloid uptake altered. Pretreatment with antihistamine drugs did not alter the rate of phagocytosis. Thorotrast was capable of temporarily suppressing gold-uptake [Barrow *et al.* (84)]. Similarly, there was no significant alteration of macrophage function in x-irradiated mice (76). Increase in the alkaline phosphatase activity of the spleen, notably with  $\text{ATP}^2$  as substrate, was observed in mice exposed to 640 r [Ashwell & Hickman (85)].

*Lymphoid tissues.*—Recent studies confirm and extend the knowledge that lymphoid tissues are among the most radiosensitive of the body. Degeneration in the lymph nodes of rats was seen within one hour after 500 r followed by profound reduction in cellularity. Regeneration to normal occurred before the seventeenth day [Metcalf *et al.* (66)]. Destruction of lymphocytes was evident in swine within 50 min. after exposure to 600 r ( $\text{LD}_{50}$ ). Marked lymphocytic destruction and phagocytosis of debris were apparent throughout the body at 3 hr. Regeneration began within 36 to 48 hr. In general, the rate and degree of injury were comparable in all lymphoid tissues [Tullis (67)], as noted in mice by Barrow & Tullis (60). Fragmentation and



lysis of the lymphoid elements of chickens were well established 1 hr. after exposure; the extent and progression of destruction were of equal intensity in all lymphoid foci. The erythropoietic elements were almost as sensitive, the myelopoietic and megakaryocytic elements slightly less in that order. The reticulo-endothelial cells remained intact [Jacques & Karnofsky (86)].

When the radiosensitivities of rat lymphocytes *in vitro* and *in vivo* were compared, the dose-effect curve plotted on logarithmic-probability paper gave a straight line. The ED 50 (dose required to produce 50 per cent pyknosis in 5 hr.) was 275 r both *in vitro* and *in vivo*. It is concluded that "indirect" effects of radiation in the body are slight or non-existent. Medium-sized lymphocytes were as sensitive as small lymphocytes. Reticular cells (macrophages), monocytes, and plasma cells were unaffected by doses up to 800 r. Whole blood was cultured and irradiated *in vitro*. The ED 50 was found to be 1600 r. Lymphocytes were therefore less sensitive in the blood than in lymph nodes [Trowell (87)]. This puzzling finding requires an explanation. Many pyknotic lymphocytes were found in the peripheral blood after 400 r, a peak of 7 per cent being reached 3 hr. after x-irradiation; they were rapidly removed from the blood stream, primarily in the lungs, where they were found lodged in the alveolar capillaries. The cytologic changes in lymphocytes are nonspecific. The small lymphocytes are nondividing cells, and the reason for their sensitivity is unknown (87).

*Thymic and lymphoid neoplasms and leukemias.*—Although it is known that all main types of leukemias can be caused by ionizing irradiation in man and the mouse, recent experimental studies are concerned only with lymphomas and usually with that type which originates in the thymus. In mice, thymic lymphomas are common, and their induction time is short. The thymus is under control of adrenal hormones and earlier studies have shown that thymectomy prevents the spontaneous development or inducibility of lymphomas originating in this gland. Studies on the induction of lymphoid tumors of mice by ionizing irradiation have been reviewed by Kaplan (88) and Kirschbaum (89). The minimal effective dose for induction of lymphoid tumors in mice is about 283 r. As the total dose is increased, there is gradual increase in lymphoma incidence, which, for a given total dose is not affected by daily fractionation. In contrast, fractionated irradiation at intervals of four to eight days yields a higher incidence, shorter latent period, and significantly steeper probitregression line. Increasing the interval to 16 days results in a decreased response. Under all treatment conditions studied, lymphoma incidence attained a plateau at about 300 days or earlier. Female mice were slightly more susceptible than males. Litters of three to four mice were significantly less susceptible than litters of five to six mice, which in turn were less susceptible than litters of seven to eight animals [Kaplan & Brown (90)].

Kaplan (91) confirmed and extended previous evidence that local irradiation is ineffective in the induction of mouse lymphoma and implicated an indirect systemic mechanism. Fractionated alternate irradiation of the upper

and lower halves of the body yielded lymphoid tumors at a rate almost identical with that of equivalent whole-body irradiation. This author postulates that irradiation releases from irradiated tissue a transient humoral material necessary for lymphoma induction, and that this material is inactivated by nonirradiated tissue. In a later study the lymphoma incidence was strikingly reduced by shielding during irradiation the thigh, lower extremity, or lower abdomen. There was a suggestive relationship between the volume of tissue shielded and the degree of protection. The lymphoma incidence was restored to high levels when the lower extremities were shielded initially and then locally irradiated afterward within 24 hr. [Kaplan & Brown (92)].

Irradiated mice given testosterone propionate had fewer lymphomas than mice given estradiol benzoate or sesame oil [Gardner (93)]. Testosterone inhibited lymphoma development in both male and female mice only when given concurrently with irradiation, the degree of inhibition being somewhat greater in spayed than in intact animals [Kaplan & Brown (94)]. Estrogens induce lymphoid tumors in susceptible strains of mice and may synergize with x-radiation [Kaplan & Brown (95)]. In a study of the influence of thymectomy, splenectomy, and gonadectomy on the incidence of radiation-induced lymphomas, 800 r was given to mice in four equal treatments at two-week intervals. Thymectomy effectively prevented induction of lymphomas by radiation, and this may be attributed simply to removal of a susceptible focus. The differences in incidence and mean induction time in gonadectomized and splenectomized irradiated and nonirradiated mice are not significant in this study [Kaplan (96)]. Injection of cortisone either concurrently with, or six weeks after, total body irradiation significantly inhibited the development of lymphomas. No tumors occurred in mice treated with cortisone alone. Cortisone failed to modify the low lymphoma incidence observed after irradiation localized either over the mediastinum alone or over the whole body with the mediastinum shielded. Bilateral adrenalectomy augmented the lymphoma incidence after total body irradiation. Adrenal cortical extract and desoxycorticosterone acetate did not influence the radiation-induced lymphoma incidence [Kaplan *et al.* (97)].

In the chronic exposure studies of Lorenz (36), leukemia developed earlier and in a higher percentage (60 to 70 per cent) of mice exposed to 8.8 r daily of  $\gamma$ -radiation than in the nonirradiated controls (40 to 50 per cent). A daily dose of 4.4 r hastened the onset of leukemia but did not materially increase its total incidence. These findings have been confirmed by Spargo *et al.* (37). The leukemogenic effect of chronic exposure of man has been amply documented by statistical analyses showing an approximately eight-fold increase among radiologists [March (98)]; that of acute exposure by the figures of Folley *et al.* (99) on the leukemia incidence in Japan (8, 13).

#### BLOOD VESSELS

Injury to vessels is scant following exposure within the total body tolerance but is marked when larger doses are administered to a localized area.

Such is the situation when particle-emitting radioisotopes are injected intravenously. The vascular changes caused by  $\text{ThO}_2$  administered to man for visualization of vessels have some resemblance to thromboangiitis obliterans and arteriosclerosis [Rotter (70)]. Thorotrast ( $\text{ThO}_2$ ) also causes the formation of tubercle-like granulomas (70). "Radiation arteritis" of the thyroid vessels is invariable following administration of  $\text{I}^{131}$  in larger than tracer doses.

Total-body x-radiation produced changes characteristic of normal aging in the arteries of young but not of old mice. The chief alterations were: increased amounts of ground substance in the vascular media, increased numbers of interlamellar fibers, and premature fraying and raggedness of the elastic fibers in the media [Smith & Loewenthal (100)].

#### RESPIRATORY TRACT AND SINUSES

The respiratory tract is relatively radioresistant, histologic changes following only massive irradiation. The characteristic changes of radiation pneumonitis, which necessitated pneumonectomy in two patients, are described as follows: pleural fibrosis, inflammation and degeneration of bronchial mucosa, followed by increase in goblet cells and loss of cilia, calcification and/or ossification of bronchial cartilage, hyperplasia of alveolar lining cells, fibrosis and a characteristic increase in elastic tissue of the alveolar walls, and formation of an eosinophilic, hyaline membrane lining the alveoli [Bergmann & Graham (101)].

Four instances of carcinoma of the nasopharynx occurred among dial painters ingesting radium and mesothorium. These epidermoid carcinomas are analogous to the lung tumors of the Schneeberg uranium miners discussed in other recent reviews (102, 113). The mucosa may have been irradiated by the  $\alpha$ -rays of the radiothorium fixed in the adjacent tissue and by the expired radon. The Rn levels of the expired air of the patients were well above the "maximum permissible amount" (10  $\mu\text{c}$ . per liter) but much less than the Rn levels in the uranium mines [Aub *et al.* (55)]. Squamous cell carcinoma developed in the maxillary antrum of a man who had retained injected  $\text{ThO}_2$  within the sinus for ten years [Hofer (103)], and a similar carcinoma of the lung developed 18 years after bronchography with  $\text{ThO}_2$ , associated with a granuloma containing granules of thorium oxide [Vogtlin & Minder (104)].

In mice exposed to total body irradiation within the tolerance range no acute changes occur in the lung, but late in life many irradiated animals develop pulmonary adenomas (13). Lorenz (36) killed mice at 11 months of age after 8.8 r daily of  $\gamma$ -radiation (total 2500 r) and found an incidence of adenoma of the lung of 75 per cent (controls 45 per cent).

Obstructive endo- and peri-tracheitis was noted in mice three to four months after administration of 35  $\mu\text{c}$ ./gm. of  $\text{I}^{131}$  [Silberberg & Silberberg (105)]. Such lesions were also noted by us infrequently in a large series of mice that had been thyroidectomized with  $\text{I}^{131}$ ; tumors or preneoplastic changes of the trachea were, however, not seen. The direct effects resulting

from  $I^{131}$  deposited in the thyroid are usually localized to parts of the trachea adjacent to the thyroid gland where degenerative changes in the cartilage and calcification are common. The obliterating tracheitis, however, uniformly affects the entire tracheal circumference.

#### DIGESTIVE TRACT

Radiotherapy for cancer of the lip was observed to produce squamous metaplasia of the adjacent mucous glands of the oral cavity in 23 patients. Metaplasia occasionally began during the first week but usually later and was extensive in the fifth and sixth weeks. The sequence of changes was hypersecretion, inspissation of secretions, atrophy of acinar cells, decrease in the number of acini, fibrosis, proliferation of cells of basal layers, metaplasia, and/or hyperplasia of cells of acini and/or ducts [Freidman & Hall (106)]. Squamous cell carcinomas of the hypopharynx and larynx, and a fibrosarcoma of the esophagus were reported in patients who received radiotherapy for thyrotoxicosis or scrofula. The latent periods were 26 to 31 years [Gooldeen (107)]. Degeneration of chief cells of the glandular stomach of mice and accumulation of inflammatory cells resulted from 600 to 1000 r. Mucous and parietal cells were increased in number. Two months later all normal cells were greatly reduced in number, and the glands were lined with surface epithelium. The only changes found after the third month were patchy fibrosis and squamous metaplasia. Ulceration of the glandular stomach did not occur [Saxen (108)]. Atrophy of the tubular glands of the gastric mucosa of the dog was produced with doses of 5000 rep administered by intragastric irradiation with  $P^{32}$  [Douglas *et al.* (109)]. Squamous cell carcinoma of the forestomach developed in a high percentage of the mice after x-irradiation with 500, 600, and 1000 r of the stomach region and subsequent feeding of 9,10-dimethyl-1, 2-benzanthracene or after the feeding of the chemical alone. No tumor developed in mice that were given x-irradiation only, and a cocarcinogenic effect of the latter is not indicated [Saxen (108)].

After exposure of rats to 250 to 1000 r there was a rapid drop in mitotic activity in the duodenal mucosa lasting for 6 hr., followed by a transient rise and then a major mitotic depression at 20 to 24 hours. Irradiation and nitrogen mustard each inhibited both division and migration but not differentiation of cells into goblet cells ("mucous degeneration"). Irradiation and nitrogen mustard combined were more effective than two comparable doses of either irradiation or nitrogen mustard. Irradiation followed by nitrogen mustard had a more pronounced action than nitrogen mustard followed by irradiation; two doses of nitrogen mustard were less efficacious than two exposures to irradiation [Webber *et al.* (110)]. Reduction of cholinesterase in the intestinal mucosa noted in rats after 500 r was maximal on the fourth day; histologically, recovery had occurred before this time [Conard (111)]. After 550 r there was a degeneration of epithelial cells in the mucosa of the gastrointestinal tract of the rat within the first 2 hr., and mitosis was inhibited for about 60 hr., after which the mucosa again appeared normal

[Metcalf *et al.* (66)]. In mice after 625 r, injury appeared within the first hour and was maximal at 5 to 32 hours. Mitosis was resumed at 3 to 4 hr., i.e., before the peak of injury was reached [Lamson *et al.* (59)]. In swine after 600 r ( $LD_{50}$ ), mitotic inhibition and necrosis of the epithelium of the crypt glands of the small bowel (ileum, jejunum, and duodenum, in decreasing order) were noted within 3 hr. Recovery occurred by 29 hr., although the rectal mucosa of some animals was still eroded [Tullis (67)]. A similar pattern of changes was observed in chickens [Jacques & Karnofsky (86)]. Adult man tolerated local doses of 4500 r of 1000 kv. x-rays administered in 54 days; ulceration, necrosis, or perforation of the colon or ileum followed 6000 to 7000 r administered in 27 to 62 days [Amory & Brick (112)].

Two days after subcutaneous injection of 250  $\mu$ c. of  $P^{32}$  in mice, there was cessation of mitosis in the epithelium of the ileum with desquamation of superficial cells. Recovery occurred by the fourth day. Desquamation of superficial epithelial cells, mucosal congestion, hemorrhage, and edema were noted in the terminal ileum and colon after 2 mc. of  $P^{32}$  [Warren *et al.* (53)]. Focal destruction of the enteric mucosa of the rat with a high energy (190 Mev) deuteron beam did not cause the acutely fatal syndrome seen within four or five days after x-irradiation of a large portion of the abdomen. Death resulted from peritonitis, hemorrhage into the bowel, or bacteremia. Chronic ulcerative bowel lesions of a progressively stenosing character were observed three to seven months after abdominal irradiation [Swift *et al.* (41)].

#### LIVER

The resistance of the liver to irradiation in all species studied is remarkable. Doses greater than 12,000 r are required to cause significant liver injury (injury of lesser degree can be caused by 2500 to 12,000 r), and even after exposure to 40,000 to 60,000 r enough liver cells remain uninjured to enable recovery although the end result is cirrhosis [Koletsky & Gustafson (113)]. The liver sensitivity of the rabbit was studied by direct irradiation with single doses ranging from 300 r to 100,000 r (90 kv.). In the lower dose range only focal destruction of liver cells was produced. Edema was most marked in the central part of the lobule and leukocytic infiltration in the portal areas. Damage was proportional to the dosage: 300 r produced only transient edema and hyperemia; 3000 r produced edema, congestion, and scattered small necrotic areas, clearing within seven days; and recovery was complete after 30,000 r, even though this dose caused marked transient destruction [Ariel (114)]. In the hamster 2000 r to the hepatic region caused reduction of cytoplasmic basophilia, glycogen, and sudanophilic fat within 24 hr. [Livingstone & McCallion (115)]. In chickens dying acutely following irradiation, the most conspicuous change was liver necrosis occurring within 2 hr. after irradiation. The delayed effects paralleled those reported for mammals [Jacques & Karnofsky (86)]. The acute fatal hepatic necrosis is a unique phenomenon. In mice, fatty degeneration of the liver following median lethal x-radiation was mitigated by administration of testosterone propio-



nate, 0.5 mg. daily, postirradiation [Ellinger (116)]. The mechanism of this effect is unknown.

Within the first week after subcutaneous injection of mid-lethal doses of  $P^{32}$  into mice, there was vacuolation of the cytoplasm of liver cells and focal necrosis. This was followed by increased mitotic activity of hepatic cells, portal fibrosis, and focal hemopoiesis [Warren *et al.* (53)]. Colloidal  $Au^{198}$  selective localizes in the RE system. Administration of 59 to 82 mc. of  $Au^{198}$  to puppies produced atrophic cirrhosis in about three months, with obliteration of hepatic veins and central fibrosis [Hahn *et al.* (117)]. Colloidal  $Au^{198}$  given intravenously to rats, 20 to 35  $\mu$ c./gm. (estimated dose 24,000 to 42,000 r), caused profound necrosis of liver cells and jaundice, followed by nodular cirrhosis without marked fibrosis. Kupffer cells, biliary epithelium, and blood vessels were not significantly injured. Liver necrosis was also produced by a single intravenous dose of 7 to 10  $\mu$ c. of colloidal chromic  $P^{32}$  phosphate/gm. body weight [Koletsky & Gustafson (113)].

#### TESTIS

The germinal epithelium of the testis is highly radiosensitive; however, it can recover from acute doses of radiation which would be lethal if delivered to the whole body. Recent studies have identified the spermatogonium as the most sensitive of the germinal cells and have measured its radiosensitivity under various conditions of exposure. Doses of 50 to 400 r in mice decreased testicular weight and spermatogenesis. Quantitative cell counts indicated that spermatogonia were principally affected by inhibition of mitosis and not by cell death. The more mature germ cells continued to divide and mature. Spermatogonia in mitosis were more sensitive than resting ones. A second dose of x-rays, 12 weeks after the first dose, produced effects identical to those of the first, indicating complete recovery in the interim. The Leydig cells and stroma were not affected by irradiation with the doses studied. The effects of 10 Mev x-rays were qualitatively similar to those of 186 kev. x-rays [Eschenbrenner & Miller (118)]. In the testes of mice exposed to a single dose of 1440 r, response was limited to the spermatogonia within 24 hr. Mitosis was inhibited for at least 24 hr., and resting spermatogonia decreased in number after 20 hr. [Fogg & Cowing (119)]. It was estimated that a single exposure of mice to 300 r destroyed approximately 90 per cent of the germinal elements, 1440 r destroyed 97.5 per cent, and 5050 r destroyed all but the Sertoli cells. Correspondingly, only the latter dose caused sterilization. Once a type of germinal element began to disappear, the rate was approximately the same regardless of the dose. After exposure to 5050 r all gonidia disappeared in five days, the spermatocytes in 10 days, the spermatids in 14 days, and the sperm in 21 days [Fogg & Cowing (120)]. After exposure of mice to 300 r, the period of least frequency of spermatocytes was 14 days, that of spermatids and sperm 28 days. It was estimated that it takes 22 days for a gonidium to develop into a sperm. Some gonidia, not in prophase when irradiated, underwent liquefaction after an attempted division [Fogg & Cowing (121)]. In the testes of rats ex-



posed to 550 r, degeneration of spermatogonia occurred within the first few hours, followed by disappearance of the remainder of the spermatogenic elements as they matured. Spermatogonia began to reappear between the 20th and 40th day. Spermatozoa from the vasa deferentia exhibited no change in motility prior to the twenty-first day, but after this time motility was reduced or absent in most cases [Metcalf *et al.* (66)]. After 1000 r, cytologic changes were detectable with the electron microscope in the spermatids and other relatively mature germ cells of the rat [Watson (122)]. Spermatogonia of prepubertal, preweanling, and newborn rats were less radiosensitive to inhibition of mitosis after 300 to 500 r, but more sensitive to irreparable damage than those of adult rats [Shaver (123)]. Total body irradiation (500 r) was more injurious to the testes of adult rats than local exposure to the same dose [Shaver (124)]. Chronic  $\gamma$ -radiation of mice at a dose level of 8.8 r daily caused a marked testicular atrophy after eight months. This dose rate produced greater injury within two months than 4.4 r daily within 16 months, indicating the relatively greater importance of dose rate than total dose [Spargo *et al.* (37)]. Doses of 1 r per day or more caused a severe injury of the testis of the dog [Metcalf & Inda (38)].

Median lethal doses of  $P^{32}$  (250  $\mu$ c.) brought about disappearance of spermatogonia in the testes of mice within nine days after subcutaneous injection. Only minimal effects were noted after 25  $\mu$ c. Interstitial cells showed vacuolation, followed by proliferation [Warren *et al.* (53)]. Marked injury to spermatogenic elements of the testis of the hamster was noted after injection of 6  $\mu$ c./gm. of  $P^{32}$  [Russ (125)]. Accidental exposure to radiations from nuclear fission caused a marked atrophy of the testes of a man 34 years old. Regeneration, indicated by repeated biopsies and sequential sperm counts, proceeded slowly [Oakes & Lushbaugh (126)].

#### OVARY

The high sensitivity of the ovary to ionizing irradiation has been amply confirmed by recent studies; it is still not known whether radiation will produce ovarian tumor in any species other than the mouse. Knowledge of the histological changes in this organ has been amplified by the use of histochemical techniques. Degeneration of granulosa cells occurred after doses of  $P^{32}$  as low as 3  $\mu$ c./gm. [Odeblad (127)]. Immediately after injection of  $P^{32}$  in sublethal doses there was a disappearance of germinal epithelial buds in the mouse's ovary with reappearance in 15 to 20 days; however, maturation of these primordia into oocytes did not occur. Degeneration of granulosa cells and oocytes was noted in the primary follicles. Secondary follicles underwent atresia at an increased rate. Fibrosis and infiltration by "interstitial glands" occurred within two to three months, with decrease in the size of the ovary [Warren *et al.* (53)]. Following chronic irradiation of mice (1.1 to 8.8 r daily), the degenerative changes in the ovary were similar to those which follow single irradiation [Spargo *et al.* (37)].

When observed until natural death, 60 to 100 per cent of mice developed

ovarian tumors after  $\gamma$ -irradiation of 0.11 to 8.8 r daily, while the incidence in the controls was 12 per cent. [Lorenz (36)]. Irradiated mice (280 to 380 r) given prolonged weekly injections of estradiol benzoate did not develop ovarian tumors, as did mice given testosterone propionate (1.25 mg. weekly) [Gardner (93)]. Irradiated ovaries implanted intramuscularly into irradiated and nonirradiated spayed mice, gave rise to many granulosa-cell tumors, luteomas, and related neoplasms; however, no such tumors occurred when irradiated ovaries were implanted into nonirradiated, nonovariectomized mice. Nonirradiated ovarian grafts in irradiated, spayed animals yielded only one sarcoma that probably did not originate in ovarian tissue. It is suggested that both a direct and an indirect mechanism are involved in the development of tumors in irradiated mouse ovaries, and that intact ovarian endocrine function inhibits the development of tumors [Kaplan (128)]. Four weeks after exposure of rabbits to 400 r there was a marked diminution in the number of ova, degenerative changes in surviving ova, and lessening of response to hormonal stimulation of the ovaries, but little if any change in the formazan uptake (succinic dehydrogenase activity) of stromal cells [Foraker *et al.* (129)]. These observations are of special interest with respect to ovarian tumor induction by ionizing irradiation. Lorenz *et al.* (36) have shown that rabbits are refractory to ovarian tumor development. The available evidence indicates that in mice, which are highly susceptible, the induction of ovarian tumors depends upon the action of gonad-stimulating hormones, to which granulosa and lutein cells of the irradiated ovary of the mouse retain sensitivity. Ionizing radiations, as used in the clinical treatment of benign gynecological conditions, are nontumorigenic for the human ovary [Speert (130)]. The customary therapeutic administration of estrogens further minimizes the likelihood of ovarian tumor induction in woman.

#### UTERUS-VAGINA

Lorenz (36) reported the development of uterine carcinoma in 11 out of 12 rabbits exposed daily to doses of 1.1 r or more of  $\gamma$ -radiation, and in two out of six nonirradiated controls. The neoplasms metastasized more widely and appeared earlier (33 to 50 months) in the irradiated animals than in the controls (57 months). The sensitivity of the rabbit's uterus to ionizing irradiation is unique, and it is possible that this tumor results from a hormonal imbalance initiated by the irradiation. Changes in the human vaginal mucosa following intravaginal radiation are similar in character to those in skin. Reaction is minimal after 7500 r. Desquamation of the epithelium and ulceration are seen after 30,000 r [Tischer (131)].

#### KIDNEY

The mammalian kidney is thought to be relatively radioresistant; however, in three children after therapeutic radiation (5200 to 6850 r) over the renal area, death from nephritis supervened within five to seven months. The

earliest, and presumably primary, changes occurred in the glomerular endothelium and basement membrane and appeared to be independent of vascular and tubular changes. The renal tissue of young, growing individuals may be more susceptible to irradiation than that of adults [Zuelzer *et al.* (132)]. Kunkler *et al.* (133) analyzed the effects of massive irradiation of the kidneys of 93 patients. Renal failure occurred after 6 to 12 months in those given 2300 r or more to both kidneys during five weeks. The microscopic changes in the kidneys resembled malignant nephrosclerosis, with diffuse interstitial fibrosis and frequently sclerosis of the perirenal connective tissue (133). A progressive nephrosclerosis, leading to renal failure, was observed in rats following intravenous injection of polonium (10  $\mu\text{c.}/\text{kg.}$ ) [Casarett (58)] and after exposure, under the protection of hypoxia, to acute supralethal doses of x-radiation [Bennett *et al.* (30)]. Neoplasms of the kidney in rats following intravenous injection of 10  $\mu\text{c.}/\text{kg.}$  of polonium included benign and malignant neoplasms, and a fibrosarcoma [Casarett (58)].

#### THYROID

Although radioresistant, the thyroid gland is readily injured by small quantities of the "thyroid-seeking" isotopes,  $\text{I}^{131}$  and  $\text{At}^{211}$ ; however, the energy expended by them in the thyroid is relatively great for the damage inflicted, as is borne out by recent studies. The progressive degenerative process observed in the thyroid glands of rats that received 300 or 525  $\mu\text{c.}$  of  $\text{I}^{131}$  consisted of: (a) degeneration and necrosis of epithelial cells with follicular disruption; (b) vascular degeneration and thrombosis; (c) acute and chronic inflammatory changes; (d) fibrous organization; and (e) epithelial regeneration. After administration of 875  $\mu\text{c.}$ , no epithelial regeneration occurred. "Viable" parathyroid glands were found in all animals, although in some, peripheral fibrosis had occurred. Tracheal damage and slight reversible changes in the kidneys were also noted. It is estimated that 18  $\mu\text{c.}$  (12,000 rep) to a point at the center of the gland over a period of nine days produces no damage, 300  $\mu\text{c.}$  (53,000 rep) injures, and 875  $\mu\text{c.}$  (150,000 rep) destroys the gland [Goldberg *et al.* (134)]. Of 10 rats sacrificed 18 months after a single injection of 400  $\mu\text{c.}$  of  $\text{I}^{131}$ , two had anaplastic, nonencapsulated neoplasms, one of which was invasive. Hürthle-like elements were evident in the parenchyma of all glands, and multiple adenomata in two [Goldberg & Chaikoff (135)]. In the thyroids of rats that had received 5  $\mu\text{c.}$  of  $\text{I}^{131}$  (5800 rep) there was definite impairment of function. A persistent increase in cell height was present for one and one-half years in animals that had received 5 to 100  $\mu\text{c.}$  of  $\text{I}^{131}$ ; bizarre nuclear changes became apparent after the administration of thiouracil. The failure of the thyroid to enlarge in response to the administration of thiouracil, in spite of the persistent hypertrophy of the cells, and the finding of only one adenoma of the thyroid in the 500 rats studied, suggest that radioiodine lowers the proliferative capacity of thyroid cells [Maloof *et al.* (136)]. Sarcoma in the thyroid region developed in a wo-

man 30 years after radiotherapy for thyrotoxicosis [Jayes & Dale (137)]. In mice, sequelae to high doses of  $I^{131}$  include: curtailment of growth, failure of thyroid function and regeneration, parathyroid injury, tracheal injury and tumors, recurrent laryngeal nerve injury, ovarian sterilization, and fatal adenohypophyseal tumors. The thyroid-destroying dose in mice is estimated to be 120,000 rep [Gorbman (138)]. These findings have been confirmed except for the development of tracheal tumors. Mating tests indicate that mice given thyroidectomy-doses of  $I^{131}$  can undergo about two normal pregnancies, after which they become sterile. Their ovaries bear a resemblance to those of irradiated mice; however, regenerative changes, such as lead to development of ovarian tumors in almost every x-irradiated mouse, are slight or absent in radiothyroidectomized mice (139). In partially radiothyroidectomized animals there is absence of thyroid hyperplasia even in the presence of TSH<sup>2</sup>-secreting tumors. The rudimentary thyroid follicles are usually embedded in excessive connective tissue; the nutrient arteries are markedly stenosed; and chronic inflammatory cells and hemosiderin are scattered at the original site of the thyroid. The thyroid cells present are poorly arranged in follicles and afflicted with varied chromatin abnormalities known to occur in heavily irradiated tissues. The parathyroid is usually identified but is smaller than normal and is slightly or moderately fibrosed, notably in the parts adjacent to the thyroid.

Suckling young deprive the mother of some  $I^{131}$  and thereby protect her thyroid gland. In suckling mice receiving 5  $\mu$ c. at three days of age the development of the thyroid gland is arrested, the epithelium remains undeveloped, and colloid secretion is suppressed. Lower doses (3  $\mu$ c./gm.) to the mother cause basophilic adenomas of the pituitary in the suckling. It is estimated that the thyroid gland of the suckling young is three times as radio-sensitive as that of the mother [Rugh (140)].

Changes in the human thyroid caused by radiothyroidectomy were described by Freedberg *et al.* (141). In euthyroid patients, no histological changes were noted seven days after administration of 17 and 20 mc. of  $I^{131}$  which delivered 14,500 and 31,000 rep respectively to the thyroid gland. Fourteen and twenty-four days after administration of 59 and 26 mc. of  $I^{131}$  a marked central destruction of the thyroid gland was noted with thrombosis and hemorrhage and polymorphonuclear infiltration. At the periphery of the gland, destruction was less severe. In the thyroid glands of those surviving longer, there were fibrosis, lymphocytic infiltration, arteriolar intimal thickening with hyalinization, and atypical epithelial cells with hyperchromatic nuclei. At 316 and 1069 days there were dense fibrosis, arterial sclerosis, and atypical epithelium, with disruption of the follicular structure. No histological changes were noted in the trachea, larynx, and pituitary gland. Mitoses were absent, and no thyroid neoplasm was noted (141).

$At^{211}$  is more effective in destroying the thyroid of the rat than comparable doses of  $I^{131}$ . Ten  $\mu$ c. of  $At^{211}$  caused profound atrophy, with fibrosis, and 50

$\mu\text{c.}$  caused complete destruction. At  $^{211}\text{At}$  is an alpha-emitter, while damage from  $\text{I}^{131}$  is caused mainly by  $\beta$ -rays and to a variable extent by  $\gamma$ -rays, depending on the size of the gland. A more selective concentration of  $\text{At}^{211}$  in the thyroid is not indicated [Hamilton *et al.* (142)].

#### PITUITARY

The pituitary is radioresistant. In mice, destruction of the thyroid by  $\text{I}^{131}$  (200 to 300  $\mu\text{c.}$ ) is followed regularly by the development of pituitary tumors [Gorbman (143)]. Radiation thyroidectomy also occurs with smaller amounts of  $\text{I}^{131}$  ( $\sim 30 \mu\text{c.}$ ) in mice on a low iodine diet but is not followed by pituitary tumor development. This raises the question whether pituitary neoplasia is attributable, in part at least, to a direct effect of ionizing radiation on the pituitary. Thyroid implants or adequate thyroxine treatment prevent the induction of such pituitary tumors (144), but not implants of pituitary, ovarian, or adrenal tissue (145). Pituitary tumors will develop after 30  $\mu\text{c.}$  in mice kept on a low iodine diet if this dose is followed by whole body irradiation (545 r). Therefore, it is postulated that ionizing radiation induces these growths in pituitaries preconditioned by radiothyroidectomy [Gorbman & Edelmann (146)]. However, it is also conceivable that the pituitary changes are secondary to irradiation of the ovary or adrenal; depression of ovarian function is likewise followed by stimulation of the basophile cells of the pituitary (147). In mice killed at eight to eleven months following destruction of the thyroid by 600  $\mu\text{c.}$  of  $\text{I}^{131}$  the histologic findings consisted of hyperplasia of the anterior lobe of the pituitary, degranulation of acidophiles, and hyperplasia of basophiles, which occasionally formed nodular clusters. The hypertrophied basophiles had foamy or finely granular cytoplasm, generally containing hyaline vacuoles; many had a single large vacuole ("signet ring" or "thyroidectomy" cells). No pituitary neoplasms were found [Goldberg & Chaikoff (144)].

In rats and dogs, radiothyroidectomy was not followed by the development of pituitary tumors. The changes occurring in the anterior pituitaries of rats were solely the consequence of thyroid destruction as they were identical with those occurring after total surgical thyroidectomy [Goldberg & Chaikoff (148)]. There are several explanations for the responsiveness of the mouse's pituitary to tumor development following radiothyroidectomy and the absence of a similar responsiveness in the other two species studied. The most plausible explanation holds that in mice the pituitary is heavily irradiated because of its closeness to the thyroid. If this is true, radiothyroidectomized men are not likely to develop pituitary tumors. Another assumption is that of species differences in susceptibility. To pituitary tumor induction by  $\text{I}^{131}$  all strains of mice tested proved susceptible and the induction rate was nearly 100 per cent, but gross tumors did not develop until about 11 months after injection of  $\text{I}^{131}$  (147).

These tumors are not autonomous neoplasms. They can be grafted on



nearly all radiothyroidectomized animals of the strain of origin but not on normal members of the same strain (139). In the course of successive passages these dependent tumors can acquire autonomy. Microscopic changes in normal hosts bearing such autonomous pituitary tumors indicate secretion of large quantities of thyroid-stimulating hormones (TSH) and lack of secretion of other hormones. Assays of blood and tumors in radiothyroidectomized hosts indicate TSH secretion in quantities comparable to those of normal pituitaries. In addition, radiothyroidectomized hosts bearing dependent tumors exhibit a marked gonadal stimulation and a cavernous dilatation of the extrahepatic biliary ducts (149). The former is explained by enhanced sensitivity of radiothyroidectomized mice to the normal gonad-stimulating hormones; the latter may be related to hormones influencing the emptying of the biliary tract. Administration of thyroid hormone to radiothyroidectomized mice will prevent or retard the growth of grafted primary pituitary tumors induced by radiothyroidectomy.

#### ADRENAL

No histologic effects in the adrenal gland specific for irradiation have been reported in the recent literature, and the organ is considered highly radio-resistant. In rats, 800 to 1000 r invokes the adaptation syndrome of Selye. There is a broadening of the acetal phosphatid-containing zone (plasmal zone) with an increase of this substance in the adrenal cortex. Pretreatment with cysteine prevents this change [Hornykiewytch (150)]. Adenomas of the adrenal medulla appeared to be more numerous in rats surviving longer than one year after intravenous injection of polonium (1  $\mu\text{c.}/\text{kg.}$  or more) than in controls [Casarett (58)].

#### MAMMARY GLAND

There are no recent reports on the histopathologic effects of radiation upon the breast, an organ of intermediate radiosensitivity. The carcinogenic effects of ionizing radiations on the mammary gland have, however, been the subject of a few publications. The relation of mammary gland tumors in mice to hyperestrogenization, attributable to incidental ovarian tumors, has been confirmed and extended. Guinea pigs also have been shown to be sensitive to the induction of breast tumors by ionizing irradiation, although in this species the carcinogenesis is unrelated to granulosa tumors [Lorenz (36)]. Chronic  $\gamma$ -irradiation of female mice caused an increased incidence of mammary gland tumor, after dose levels of 0.11 r daily to 8.8 r daily, from 0 per cent in controls to over 20 per cent in all irradiated groups. Similarly 47 per cent of female mice free of the milk agent developed mammary tumors after 8.8 per r day, as compared with 4 per cent of controls. The incidence of carcinomas was approximately 20 per cent and of sarcomas 30 per cent. Most of these tumors were associated with ovarian tumors, usually of granulosa cell type [Lorenz *et al.* (151)]. An increased incidence of



carcinomas and fibrosarcomas of the breast was observed in mice and rats as a late consequence of total surface  $\beta$ -radiation after doses of 4000 to 5000 r.e.p. [Raper *et al.* (152)]. Mice born of low mammary tumor strain females were x-rayed by Andervont & Dunn (153) to ascertain whether they harbored a weak or masked mammary tumor-agent. There were no significant differences in tumor development in the offspring born to irradiated and nonirradiated mothers.

#### SKIN

Injury to the skin from x-rays and radium was the first radiation hazard discovered. Carcinoma arising at sites of radiation burns killed many early workers with x-rays and this hazard has not yet vanished [Mohs (154)]. In an analysis of 121 human cases of radiodermatitis, the epidermal changes consisted of atrophy, acanthosis, hyperkeratosis, parakeratosis, dyskeratosis, and dysplasia, with gradations leading to carcinoma *in situ* or infiltrating carcinoma. In late stages melanoderma was usually present. Intraepidermal or subepidermal edema was common, persisting as long as 18 months postirradiation. The vascular changes included swelling and vacuolation of endothelial cells and of the smooth muscle of the arterial media. The media and adventitia of arterioles underwent hyalinization; there was perivascular lymphocytic infiltration and edema. Endothelial proliferation resulted at times in obliteration of the vascular lumen, often with thrombosis. Telangiectasia in the dermis usually occurred after the acute changes had subsided. The vascular changes were the most characteristic and consistent features of radiodermatitis but were typically focal and irregular within the irradiated area. Stromal changes were nonspecific, consisting of acute inflammation, followed by chromotropic and fibrinoid degeneration of collagen, hyalinization, and fibrosis [Teloh *et al.* (155)]. In over 1400 patients who had previously received superficial radiation of the skin for dermatoses, total doses up to 1000 r did not produce any sequelae; larger doses produced radiodermatitis in about 28 per cent of the cases [Sulzberger *et al.* (156)]. Mast cells in the dermis of human patients became degranulated following deep x-irradiation, with extrusion of their metachromatic substance into the surrounding connective tissue. It was speculated that this phenomenon might represent secretion of a heparinoid material [Novaro (157)].

The effects of soft (100 kv.) roentgen rays on the rabbit skin were found to be superficial. No erythema was detected below 2700 r. Doses of 7000 to 14,000 r caused atrophy of the epidermis, hair follicles, and adnexal glands, and degenerative changes extending as deep as the muscular coat of the cutis. They healed with fibrosis and disappearance of rete pegs. Slight regrowth of fine white hair occurred after 7000 r but not after 14,000 r [Christensen *et al.* (158)]. The histologic and chemical alterations produced in the mouse epidermis by 3000 r of soft x-rays (50 kv.) were compared 21 days postirradiation with those caused by methylcholanthrene. Both treatments were as-

sumed to be carcinogenic. The histologic changes and deficiencies in essential components of the epidermis (calcium and total lipids) were similar. The basal cell region was injured most. Both treatments increased the relative number of differentiated cells. Dividing cells were more numerous after methylcholanthrene treatment [Toosy (159)].

Irradiation from superficial plaques of sulfur<sup>35</sup>, cobalt,<sup>60</sup> cesium,<sup>137</sup> yttrium,<sup>91</sup> strontium,<sup>90</sup> or yttrium<sup>90</sup> produced three principal types of lesion in porcine skin: (a) epidermal atrophy (subclinical), which appeared one to two weeks postirradiation and lasted only two to three weeks; (b) exfoliative dyskeratosis usually preceded by erythema and followed by epilation and chronic radiation dermatitis; and (c) ulceration; surface dosages twice or more than those required to produce dyskeratosis often resulted in trans-epidermal necrosis with ulceration of the entire target area. Healing was slow, followed by chronic radiodermatitis [Moritz & Henriques (160)]. Mice irradiated by external  $\beta$ -rays from P<sup>32</sup>, in single total surface doses of 5000 rep, showed effects upon the skin similar to those resulting from x-irradiation. Typical radiation effects were noted also in the superficial portions of the spleen and testis, and in the bone marrow of phalanges. (The half-thickness of this  $\beta$  in tissues is 0.76 mm. [Snider & Raper (161)].) Irradiation with x-,  $\gamma$ - and  $\beta$ -rays inhibited mitoses in the skin of the nipple of the guinea pig; estrogenic stimulation increased the sensitivity of the skin. The threshold dose for mitotic inhibition was 400 r. Fractionation of 2400 r led to diminution of its effect [Jadassohn *et al.* (162)].

Experiments indicating a hitherto unsuspected resistance of epidermal cells to  $\alpha$ -rays have been reported by Devik (163). Some cells of the epidermis of hairless mice will survive doses of the order of 100,000 rep of  $\alpha$ -rays from polonium spread on a nickel sheet with a tissue depth range of approximately 37  $\mu$ . The mitotic activity is suppressed for one to two days. The characteristic cytologic changes of x-irradiation, such as chromosome fragmentation, "bridges," and micronuclei, were only occasionally observed after the  $\alpha$ -irradiation. The sequence of changes noted was as follows: at 6 hr., swelling and pyknosis of nuclei; at 12 hr., marked swelling of the epidermis; at two days, necrosis; at six days, both atrophy and swelling of the epithelium; and at 20 days, atrophy of the epidermis. The differences in effect on the skin between x-rays and  $\alpha$ -rays are explained by lack of irradiation of structures subjacent to the epidermis by the  $\alpha$ -rays. Irradiation of the latter, it is assumed, has an indirect deleterious effect on the epidermis (163). If a polonium-impregnated nickel plate is inserted subcutaneously, the epidermis undergoes hyperplasia, rather than atrophy. Likewise, the vascular changes are more prominent with this "internal" irradiation [Kreyberg & Devik (164)]. The relative efficiency of the 23 Mev betatron compared with 200 kev roentgen-ray irradiation was 0.56 for erythema, 0.67 for epilation of the rabbit skin, and 0.60 for destruction of human tumors [Haas *et al.* (165)]. Thermal neutrons were equally effective in inhibiting mitoses in the

skin of the mouse, as in producing acute death, the relative biological effectiveness being 1.7 in each instance, as compared with x-radiation [Storer (166)].

The sensitivity of the hair follicle of the rat to soft x-rays (44 kv.) during the various phases of the hair cycle was thoroughly investigated by Geary (167). The median effective dose of radiation capable of producing complete local epilation was 1720 r on the fifth day of the cycle, 1315 r on the tenth, 1030 r on the fifteenth, 1750 r on the twentieth, and 1740 r on the twenty-eighth day. Maximum sensitivity to radiation occurred during the active phase, on the fifteenth day, while the period of minimal sensitivity corresponded to the resting phase, on the twentieth or the twenty-eighth day. Regrowth of hair six weeks after exposure to 2000 r was more nearly complete if the exposure was carried out during the resting phase. The matrix cells of the growing follicle were among the most sensitive elements in the skin, while the dermal papilla was relatively radioresistant. Temporary epilation was associated with damage to the hair follicles, and permanent epilation resulted from failure of the follicles to regenerate, attributable to destruction of the dermal papilla. Higher doses were required for permanent epilation than those capable of producing temporary loss of hair (167).

Greying of the hair following x-irradiation was studied extensively by Chase *et al.* (168). It is postulated that the hair pigment originates in the potentially pigmented dendritic cells (melanoblasts) which supply the matrix cells with the basic pigment granules or their precursors. All white hairs result from destruction of the dendritic cells. Partially pigmented hairs are the result of either partial inactivation of these cells, with retention of some melanogenic function, loss of cell divisibility, or destruction of some of these cells. In the mouse the degree of greying depends on the dose the dose rate, and the stage and size of hair follicle. The threshold dose in the mouse and hamster is 200 r. The permanency of radiation effect indicates that there is little if any postembryonal migration of melanoblasts. Late embryo and newborn mice develop less greying than adults exposed to the same dose, presumably because of new formation of follicles with incorporation of the initial supply of melanoblasts, which is not replenished in late life (168, 169). Local subcutaneous injection of certain carcinogens and cytotoxic substances simulate radiation in producing greying of hair through injury of melanophores [Boyland & Sargent (170)].

While most of the epitheliomas arising in radiodermatitis are of the squamous cell type, in 11 cases basal cell carcinoma developed in an area of chronic radiodermatitis. Most of the cancers occurred on the face; basal cell carcinoma does not follow irradiation of palms, soles, or mucous membranes. The period of latency varied from eight to fifteen or more years [Anderson & Anderson (171)]. Single total surface doses of 4000 to 5000 rep of  $P^{32}$  led to skin tumors in mice and rats. Neoplasms began to appear within four months, and by the end of one year each animal averaged twelve cutaneous

tumors, including squamous and basal cell carcinomas [Raper *et al.* (152)]. A squamous cell carcinoma developed on the eyelid of a man 35 years following injection of  $\text{ThO}_2$  into the lacrimal duct. The excised tissue contained an estimated  $5 \times 10^{-3}$  gm. of thorium which was estimated to deliver 1.5 r/day or 20,000 r in the 35 years (the cited tolerance dose is 0.25 r/day) [Rudolphi (172)]. Squamous cell carcinoma of the face developed after a latent period of 254 to 354 days in 3 of 19 rats that had been given a large internal dose of  $\text{P}^{32}$  [Koletsy *et al.* (173)]. A fibrosarcoma developed in the area of radiodermatitis in a man who had been treated with radium 20 years previously for carcinoma of the lip [Stewart & Pendergrast (174)].

### EYE

The development of cataracts among cyclotron workers and Japanese exposed to atomic bomb radiation has stimulated research on cataractogenesis by ionizing radiations. The lens of the mouse has been found sensitive to doses as small as 15 r [Upton *et al.* (175)]. The relatively high effectiveness of neutrons in cataract induction has been confirmed [Christenberry & Furth (176)], [Cogan *et al.* (177)], [Storer & Harris (178)]. The cytology of radiation cataract was studied by Von Sallmann (179). Unilateral x-radiation (1500 r) produced complete inhibition of mitosis of cells of the anterior epithelium of the rabbit's lens within 30 minutes lasting three to four days and followed by periods of recovery and mitotic hyperactivity, persisting a week or more. Nuclear abnormalities appearing within 2 hr. after irradiation were more conspicuous at the time of resumed mitosis, especially during the "overshooting," and in the germinative portions of the lens epithelium. Nuclear degeneration led to vacuole-formation and cytolysis. Cysteine delayed the mitotic recovery, reduced the "overshooting," and lessened the nuclear damage (180). In rabbits, doses of 2000 r to the eye led to opacities in 4 to 10 weeks. Fractionation of the dose delayed the opacities. Nuclear degeneration was observed within the first week, swelling, granulation, and vacuolation of fibers in the subcapsular region within three weeks (181). Cogan & Donaldson (182) described the accumulation of degenerated epithelial cells along the posterior suture in the rabbit lens which, they believe, migrated to this location after injury and contributed to the formation of the opacity. Experiments with radioactive tracers indicated increased permeability of the cataractous lens of the rabbit, but this change accompanied rather than preceded the development of cataracts [Von Sallman & Locke (183)]. Permutt & Johnson (184) found the following histochemical changes in the rabbit lens following radiation injury: swelling of the capsule, the lenticular fibers, and the cement substance, and an increased reaction with the Hotchkiss polysaccharide stain and increased solubility of the polysaccharide-protein complexes. These changes were interpreted as resulting from depolymerization of the polysaccharide-protein complexes of the lens in a manner

similar to the breakdown by radiation of polymers *in vitro* or occurring secondary to injury of epithelial cells.

Early changes (hemorrhage, edema, and infections) in the eyes of pigs and goats receiving irradiation from atomic fission were regarded as results of bone marrow depression and secondary systemic changes, rather than direct effects of the rays. The secondary effects of fission and roentgen radiation were similar, and there were no ocular changes which could be attributed unequivocally to direct irradiation [Wilder & Maynard (185)]. Similar observations were made on lenses of Japanese atomic bomb-exposed victims who died soon after exposure (186). Later, about 150 exposed people developed radiation cataracts, described in several clinical studies. Histologic changes have been correlated with the clinical findings in the lens removed from a 22 yr.-old man five years after the bombing of Hiroshima. The posterior capsule was thickened in the form of a sharply demarcated band. Epithelial cells at the equator had irregular and bizarre nuclei. Many fibers were vacuolated and replaced by eosinophilic, amorphous, granular material. In the posterior polar region there was a space containing amorphous debris [Kimura & Ikui (187)]. The histologic features of human radiation cataract, resembling those of the rabbit, are degenerative changes of the anterior epithelium of the lens, associated with retrogressive changes and vacuolation of fibers in the posterior cortex. In the advanced cataract there may be complete disappearance of epithelium and lysis of the cortex [Cogan *et al.* (188)].

The high radiosensitivity of the developing eye is indicated by the studies of Lorenz & Dunn (189), who found advanced cataracts, severe retinal atrophy, and vascularization of the cornea in all mice surviving one year after 400 r given at birth. The epithelium of the cornea is radiosensitive as judged by effects on mitosis. Friedenwald & Sigelman (190) found the period of mitotic inhibition produced by x-irradiation subject to considerable modification by pharmacologic measures, such as anaesthesia, atropine, and BAL (British anti-lewisite). They were unable to reconcile their data with the traditional "target" theory and postulated the intermediate action of a chemical "vector" to account for the observed effects of radiation on chromosomes.

#### BONE AND TEETH

While mature bone and teeth are radioresistant, growing human bone is highly sensitive. Over the epiphyseal line, 440 r or more resulted in deformities and retardation of growth of long bones; however, doses of 275 to 300 r, even if repeated, produced no permanent alteration [Montag (191)]. The spine of growing children is thought to tolerate up to 2000 r, but radiation in excess of 2000 r is productive of growth disturbances. The morphologic changes include nonspecific growth retardation and irregularity of ossification of epiphyseal cartilage [Neuhauser *et al.* (192)]. In hamsters dying three to four days after exposure to 1500 r, there is fibrosis of the bone marrow, with loss of osteoblasts, loss of metachromasia of the fibers, and formation of



a massive network of reticulum. Loss of osteoblasts was observed as early as 3 hr. after irradiation with 110,000 r. These changes are similar to those reported earlier in other species [Levy & Rugh (193)].

When thorium X and platinum, combined, were administered to rabbits, each was found to be deposited independently in organs of their predilection. ("Petosthor," a combination of thorium X with platinum sol and eosin blue, has been used in the treatment of bone and joint diseases.) Platinum was demonstrable only in the liver. Thorium X disturbed endochondral ossification, retarded longitudinal growth of bones, caused calcium depletion and spontaneous fractures, and was taken up by the placenta, causing premature birth in pregnant animals [Koch (194)]. The high sensitivity of growing bone to direct irradiation was the subject of an editorial in Radiology [Jacox (195)]. Major factors in bone injury are vascular damage and diminished recuperative capacity. Damage to osteoblasts and osteoclasts is considered of minor importance. Osteoblasts are more radiosensitive than osteoclasts. Hyperemia following irradiation may enhance decalcification. Stress is an important factor in the origin of fractures of x-rayed bones. In evaluation of sensitivity it is to be considered that the energy absorption of bone for 200 kv. x-rays is about that of soft tissues (195).

While cancer of the skin has been generally accepted as a frequent late complication following roentgen-ray burns, radiation cancer in tissues underlying the skin has been emphasized only recently. While fibrosarcomas of soft tissues have been reported, sarcoma of bone incidentally included within the field of roentgen-ray therapy appears to be more common. An osteogenic sarcoma arose in the lumbar vertebrae four years following 4400 r to this area [Spitz & Higinbotham (196)]. Another extraskeletal osteogenic sarcoma is reported in soft tissues of the back after 4000 r given in ten exposures during 70 days [Auerbach *et al.* (197)].

In 30 persons with radium and mesothorium poisoning the increased tumor incidence (25 to 33 per cent) and average latent period (19.5 to 24.6 years) showed little variation with different degrees of radioactivity (Group I, 8 to 23  $\mu$ g. of stored radium; Group II, 2 to 7  $\mu$ g.; Group III, 0.7 to 2  $\mu$ g.). All but one of these patients had "radiation osteitis." "Jaw disease" (16 cases), causing the most frequent initial symptoms, resulted from destruction of the alveolar crest and superimposed infection. The pathogenesis of the bone lesions is not understood. The bone destruction (except for the jaw bones) is an aseptic form of necrosis. Death of osteocytes is followed by bone resorption, sometimes with pathological fractures [Aub *et al.* (55)]. Bone necrosis is not localized entirely to regions of greatest alpha activity, an observation made also in other cases of radium poisoning (198). Damage of afferent arteries may have contributed to bone necrosis. The fractures usually healed fairly well. Of the eight neoplasms four were primary bone tumors, one was a fibrosarcoma of the joint capsule, and three were epidermoid carcinomas of the nasopharynx. The amount of mesothorium, age at time of ex-



posure, and mode of exposure probably modified the course of illness (55).

Osteogenic sarcomas, developing in 10 of 34 rats that were given single or repeated doses of  $P^{32}$  (4.5 to 12  $\mu\text{c.}/\text{gm.}$  body weight) occurred in different bones, most frequently in the jaw, and metastasized to the lungs. The latent period was 160 to 314 days. Osteogenesis was marked in both primary and metastatic growths [Koletsky *et al.* (173)].  $P^{32}$  (15 to 60  $\mu\text{c.}/\text{gm.}$ ) given subcutaneously to young mice resulted in disturbances of odontogenesis and osteogenesis of the mandible. The odontoblasts appeared more sensitive than the ameloblasts [Burstone (199)]. Similar disturbances could be produced by injecting adjacent to the developing jaws suspensions of insoluble chromic phosphate containing  $P^{32}$  (200). Administration of  $P^{32}$  to pregnant mice resulted in disturbances of osteogenesis and odontogenesis in the offspring. The dosages required to produce these changes were less than those required to produce similar changes in immature mice. With dosages of 10 to 17  $\mu\text{c.}/\text{gm.}$  of body weight of mother, there was cessation of histodifferentiation of ameloblasts and odontoblasts. Development of the third molar tooth was completely inhibited. Alterations in the condyle were indicative of an abnormal premature aging process. Aplasia of marrow, premature subcartilage linkage, and decreased osteoblastic activity were characteristic associated changes. The degree of damage was dependent upon the stage of histogenesis and morphogenesis of the dentition (201).

#### NERVOUS SYSTEM

Not all cells of the nervous system are radioresistant as hitherto thought. During development many nerve cells are highly radiosensitive. Irradiation of rats and mice (3 to 12 months old) caused acute necrosis of scattered oligodendroglia cells, subependymal cells, retinal rod cells, and occasional neurons in the pyramidal lobe and olfactory brain. Subependymal cells were sensitive to 200 r, but the other cells were not destroyed by doses below 1200 r. Protargol and myelin stains revealed no change in the axis cylinders or myelin adjacent to damaged oligodendroglia cells. No change was noted in the sympathetic ganglia; in the spinal cord only occasional oligodendroglia cells were injured [Hicks & Montgomery (202)]. In guinea pigs 450 to 1200 r failed to produce changes in the nucleoprotein concentration of neurons, as determined by Fuelgen staining [Beffa (203)].

Rat embryos exposed to 25 to 200 r on the ninth day of gestation developed discrete tumor-like growths in and around the brain. The incidence of such tumors was directly related to the dose. They first appeared on the second day after irradiation and thereafter exhibited varying capacities for growth and differentiation. Some grew for one or two days, others longer, but few remained in newborn animals, and these were small and gave no evidence of proliferative activity. Although the tumor-bearing animals had a somewhat higher mortality than the nonirradiated controls, neither prenatal nor postnatal death could be attributed to the presence of the tumors [Wilson

*et al.* (204)]. These changes may represent tumor-like developmental disturbances rather than neoplasms.

#### CONCLUSION

This survey of recent literature discloses a trend to correlate radiation sensitivity with nucleic acid synthesis and enzyme activity. Further advances in the histopathology of radiation will be facilitated by further utilization and development of histochemical procedures. With respect to early injury there is remarkable similarity in the behavior of different species. Carcinogenic response, on the other hand, varies so widely with species and strains that the liability of man to develop certain neoplasms will be learned probably only from observations on man. On closer survey a sharp difference is noted between neoplasms that are due to a local action (e.g., of skin and bone) and those that are dependent, in part at least, on an indirect mechanism (e.g., of ovary and other endocrine organs, and possibly leukemia). All species appear to be susceptible to the former which future research may relate more quantitatively to ionization events. The latter neoplasms may be related to species differences in the function or responsiveness and interrelation of different organs.

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## CELLULAR RADIOBIOLOGY<sup>1,2</sup>

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The title "Cellular Radiobiology" covers a broad field merging gradually into radiation physics and chemistry at one end, and into the multicellular aspects of radiation biology at the other end. It has therefore been necessary to make somewhat arbitrary choices as to the topics and individual papers reviewed. Many worthwhile contributions have been passed by, especially in the field of radiation genetics. However, this topic has been reviewed recently by Breider (34), Catcheside (47, 48), Howard (123), Kimball (131), Plough (195), Ulrich (263) and in "The Symposium on Radiobiology" (183). Major emphasis has been on the literature from 1952 dealing with the effects of ultraviolet and ionizing radiations. A few earlier references are also included where their content seemed appropriate. Because of space limitation, we shall not review per se topics dealing with the primary physical events and the formation of reactive chemical species. For those interested in these topics, we refer to numerous papers in the reports of several conferences (81, 183, 252, 253) and a review by Magee (163) in this volume. Recent reviews of cellular radiobiology are those of Errera (78), Errera & Herve (79), Gowen (103), and Sparrow & Rubin (240). A number of articles of interest to cellular radiobiologists can be found in the report of the "Fifth Josiah Macy Conference" (158).

Before considering the main body of literature we would like to outline our version of what we consider to constitute a complete description of radiation effects on a cell.

First, would be a consideration of physical loss of energy by photons and particles as they traverse biological matter. Secondly, one must know the intervening steps in the degradation of this energy to thermal energy. On the one hand, there are the degradative processes within a biological molecule which has directly received the energy from the radiation source, and the effect of these processes on functions which that molecule performs. On the other hand, there are processes resulting from the highly reactive chemical species which are formed either as the direct result of the primary physical interactions or as the end product of a degradation of the energy of a primary event within a molecule. Thirdly, one must follow these damaged or reactive molecules into the metabolic pattern of the cell and describe the changes

<sup>1</sup> The survey of the literature pertaining to this review was completed in December, 1952.

<sup>2</sup> The following abbreviations are used: DNA for deoxyribonucleic acid; IAA for indol acetic acid; RNA for ribonucleic acid.

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that they cause in the morphological or functional pattern. It is obvious that this presumes one has, in turn, a description of this pattern, which would be presuming a great deal, since this is one of the primary objects of the whole science of biology. Lastly, one would describe the observable end-results of the radiation on the cell in terms of the first three subdivisions of this outline.

We have some knowledge of the primary physical events and chemical processes that are possible in matter, following radiation, and we can make measurements of alterations in an observable cellular property. However, as emphasized by Zirkle (278), tracing the course of events between these two extremes is the difficult task. There are two general methods of attack. One method is to study cellular molecules or structures *in vitro* and from knowledge gained therefrom to synthesize a picture of the processes *in vivo*. The second method is to observe the effect of irradiating cells *in vivo* as a function of modifying conditions during the experimental procedure in the hope of using such indirect data to infer the intermediate processes. The topics reviewed will fill mainly into categories corresponding to these two general methods of attack.

#### EFFECTS ON MACROMOLECULES

The study of enzymes and other macromolecules is of interest because of the importance of large molecules in biological systems in general. Desoxyribonucleic acid (DNA) in particular, because of its presence in genetic structures, has been rather extensively studied. Koenig & Perrings (138) find that the sedimentation constant increases with low doses and decreases with higher doses of x-rays. Heavier components which appear after low doses disappear with continued radiation. Errera (75, 78) and Conway & Butler (54) have studied the slow drop in viscosity in DNA solutions that occurs after x-irradiation. The latter authors believe this is attributable to instability introduced in the molecule by  $H_2O$  radicals during the irradiation. However, Errera has shown that glutathione can protect against this viscosity decrease if added after the irradiation. Weiss (270), and Scholes & Weiss (222) have discussed these viscosity changes and attribute them to loss of hydrogen bonding through oxidative radical attack on the amino and hydroxyl groups. They believe their chemical results from x-irradiation studies in dilute solution indicate degradation of the DNA molecules by destruction of the constituent bases, fission of glycosidic linkages with liberation of free purines, and liberation of inorganic phosphate by breaking the ester linkages. Errera (76, 77) studied the ultraviolet photochemistry of DNA<sup>2</sup> and nucleoprotein. The quantum yield for viscosity change is on the order of  $10^{-6}$ . He finds that the pyrimidine bases are destroyed. Degradation to much smaller molecular units does not occur, however, thus indicating that viscosity changes are to be found in configuration changes. Rice (207), who studied the effect of ultraviolet on the reactivity of sugars, nucleosides, and nucleic acids, concludes that extensive damage occurs to the sugar

molecule in DNA. Alexander & Fox (5, 6) have used polyacrylic and polymethacrylic acids as models behaving like DNA in order to distinguish shape changes from molecular weight changes. They found that the viscosity changes are attributable to molecular weight changes with x-rays but attributable to shape changes with nitrogen mustard.

Besides the evidence for DNA, mentioned above (138), the polymerization of two other macromolecules by radiation has been reported. Carroll, Mitchell & Callanan (46) have found polymerization with no degradation in serum albumin solutions. The polymerized product has lower thermal stability than the original material. Solutions of fibrinogen (218) and dry fibrinogen (137) irradiated with x-rays both yield products of higher molecular weight mixed with lower weight fragments.

Fricke (90, 91) has studied the heat-denaturation properties of x-irradiated egg albumin, in solution and dry, and finds three different product species with different thermal properties. Kaplan & Fraser (129) exposed the same substance, in a monolayer on an aqueous surface, to ultraviolet radiation, and found that the area of the monolayer was a function of dose. They attribute this to unfolding of the albumin molecule after low doses and fragmentation after high doses.

Appleyard (12, 13) has studied the absorption spectrum, the effect of pH on solubility, and the sedimentation properties of dried hemoglobin following irradiation with electrons and with deuterons of varying ion density. He found the heme group to have a stability in the order of magnitude of that expected on the basis of its size, and that the principal damage to the protein seems to be creation of insolubility. The molecular weight of the pneumococcus transforming principle has been estimated at 6,000,000 by Fluke, Drew & Pollard by using a combination of deuteron and electron inactivation (85).

Barron has reviewed his work on the irradiation of solutions of sulphhydryl dependent enzymes (20). The role of solvent radicals in inactivating dilute solutions of enzymes has been considered by Dale (59, 60). Bier & Nord (25) found that the sensitivity of trypsin solution to x-rays was dependent upon the concentration and nature of the buffer, pH, and temperature, but not upon  $\text{Ca}^{++}$  which acts as a stabilizing factor for unirradiated trypsin.

Invertase (197), catalase (226, 228), and urease (227) have been studied in the dry state with deuterons and electrons as a function of energy-loss of the bombarding particle and temperature at bombardment. The data are consistent with a description of biological inactivation as the result of one primary ionization event occurring within the molecular structure associated with the activity. The size of this molecular structure shows, in many cases, a relation to the molecular weight as determined by other physical and chemical means. For example, in the case of invertase, diffusion measurements lead to a dry molecular weight of 120,000 as compared to a radiation-determined weight of 123,000. The temperature dependence of the inactivation of catalase is especially interesting. There are three different regions of

constant sensitivity over a considerable temperature range, corresponding to molecular units which are in size respectively, one-quarter, one-half, and the whole of the molecule.

The ultraviolet inactivation of lysozyme was carried out by Shugar (231). The quantum yield was .024 over the whole pH range tested, 3.6 to 12.0. He finds no evidence of splitting out of any amino acids or peptides. No protection was afforded by cysteine in this S—S enzyme as compared to that which occurred for —SH enzymes [Shugar (230)]. McLaren, Doering & Philips (161) have found that the intensity of radiation has no effect on the ultraviolet inactivation of pepsin by increasing the intensity 100,000 times over that used ordinarily.

#### EFFECTS ON VIRUSES

Although viruses are not generally considered to be normal cellular constituents, they are studied with interest not only for their own sake, but in the hope that they exhibit some behavior similar to cellular processes and thereby give us a clue to such processes. This is true also of radiation studies on viruses. Work in this field in the past year has been restricted largely to bacterial viruses.

Guild (108) concludes from studies with very soft x-rays that excitations of phosphorus atoms in *Escherichia coli* bacteriophage T1 are no more damaging than excitations in any other atom.

Adams & Pollard (1) have studied the dry inactivation of *E. coli* bacteriophage T1 as a function of temperature at the time of irradiation with deuterons and x-rays. Through a large temperature range at low temperatures the cross section is essentially constant but above 40°C. rises rapidly with temperature. They point out the unlikelihood that this is merely heat inactivation resulting from degradation to heat energy of the radiation energy delivered to the phage. The rapid increase in inactivation with irradiation in 3 per cent broth between 45°C. and 64°C. argues that effects in such solutions are not dependent on diffusion processes.

Buzzell & Lauffer (38) found no alteration of the rate constant for thermal inactivation following x-irradiation of *E. coli* bacteriophage T5 in 4 per cent broth. They point out that this is only suggestive, but not conclusive proof, that under conditions which should give direct effect [(Luria & Exner (154)] the first radiation event causes the lethal damage. In dilute broth, there is among the survivors, a group of phage which are more thermally sensitive. This last result is representative of a general type of study initiated by Watson (267) in which one attempts to dissociate various types of radiation damage from each other by testing for variously altered properties in the same system. Watson (268) reported further work on bacteriophage inactivated by indirect mechanisms. He distinguishes between inactivation by two groups of agents, one of which is short-lived, the other relatively stable. Phages inactivated by the former, have a greatly reduced capacity to adsorb, whereas this is not true of phages damaged by the latter agents. Alper (9, 10)



observed the same two types of indirect inactivation and attributed the delayed inactivation to the action of peroxides on phage which have been rendered less stable but not inactive by the short-lived reaction. Fredericq (88, 89) found no difference in the kinetics of the ability of ultraviolet-irradiated phage to kill bacteria when assayed on two different strains, one of which normally allows phage multiplication and one which does not. Bachofer & Pottinger (18) have reported a type of protection against inactivation in aqueous solutions which does not appear to be attributable to competition for the active radicals in solution but rather to some alteration in the state of hydration of the phages. They found that a large degree of protection is afforded by the presence of high concentrations of ammonium sulfate.

Benzer (24) has repeated the experiments of Luria & Latarjet (155) on following the intracellular growth of bacteriophage by the sensitivity of infected bacteria to form phage plaques after ultraviolet irradiation. He found that T7 phage differs considerably from T2 or T2r since its pattern of response would indicate an increasing multiplicity throughout the development period.

The phenomenon of induced lysogenesis, whereby a physical agent is able to initiate the process of phage production and liberation in a strain of bacteria which is not otherwise susceptible to phage, has been investigated by several authors. Ultraviolet light, besides its initiating effect, has been shown to affect the growth rate during the latent period, the length of the latent period, and the burst size (232, 269, 271). The effect of visible light and temperature on reversing the ultraviolet action has been studied (43, 44, 49). Induction can take place in starved bacteria, but nutrient must be provided in order for it to be observed (31). Latarjet has shown that x-rays can induce lysogenesis and, contrary to any other known case, the effect can be completely overcome with subsequent visible light (145). Kellenberger (130) has described nuclear changes in bacteria induced by ultraviolet as revealed by electron microscopy. All the cells in a culture undergo similar changes in granularity but only some of them lyse, while others revert to their preinductive vegetative state.

#### EFFECTS ON CELLULAR BIOCHEMISTRY AND PHYSIOLOGY

A number of investigators have analyzed irradiated cells in a search for damage at the chemical level. A general consideration of the study of cell components affected by radiation has been made by Dounce (69). A number of enzyme systems, particularly respiratory enzymes, have been studied in the past year. Aldous & Stewart (3, 4) have found no effect on either ultraviolet or 2 Mev x-rays on the catalase and alcohol dehydrogenase activities of yeast, but a definite decrease exists in hexokinase, carboxylase, and zymase activity. The stability of intracellular catalase is further attested by a reduction of only 30 per cent in its activity by doses of 3 Mev electrons sufficient to inactivate completely a culture of *Micrococcus pyogenes* with an

initial concentration of  $2 \times 10^8$  per ml. (197a). An interesting observation is that of Blinks (28), who reports a greatly enhanced catalase activity, presumably an adaptive phenomenon, in three genera of marine algae one year following atom bomb explosions at Bikini. Malic dehydrogenase, succinoxidase, and cytochrome oxidase were reported to be unaffected in organs following lethal whole-body irradiation of mice (15) and rats (256). Decreases of 30 to 40 per cent were reported in succinic dehydrogenase and adenosine triphosphatase activities. Increases in  $Q_{O_2}$  and  $Q_{CO_2}$  in potato tubers following x- and gamma radiation, but no accompanying changes in cytochrome oxidase or tyrosinase activity, were reported by Sussman (248). Billen & Lichstein (26) found no depression in existing levels of formic dehydrogenase in *E. coli* following 90,000 r of x-radiation, but they did find that the cells lost their ability to synthesize the enzyme in the presence of substrate. It is as difficult to draw any definite conclusions about these effects as it is about the whole field of radiation on respiratory metabolism (30). Barron has been attempting to correlate his *in vitro* experiments on the sensitivity of sulphhydryl enzymes (20) with the role such enzymes play in respiratory metabolism (21). Since the behavior of *Arbacia* eggs with respect to thiol reagents is similar to the effect of x-rays on respiration, an increase being observed at low doses and a depression at higher doses, he feels that the respiratory effects of radiation are attributable to oxidation of thiol compounds in the cell.

A problem arises in testing for metabolic derangements following radiation in tissues from multicellular organisms. The indirect physiological control which certain tissues exert on others makes it even less likely than in single cells that one can connect the primary result with the final effect. DuBois, Derooin & Cochrane (70) have shown that derangements which occur in oxidative citrate metabolism *in vivo* following x-ray and nitrogen mustard failed to occur *in vitro*. Klein (136) finds that the depression of oxygen uptake that occurs *in vivo* 24 hr. following x-radiation does not occur *in vitro*. The same results are true of the depression in the cholinesterase level of the small intestine (52) and the alkaline phosphatase level of bone (185).

Further examples of the derangements in nucleoprotein metabolism which follow radiation have been presented by a number of workers during 1952. Decreases in intestinal nucleoprotein (82), bone marrow, and spleen DNA (156, 168), mammary carcinoma and liver DNA (128), and lymph gland and thymus DNA (272) have been reported. Isotope uptake studies confirm this decreased synthesis. The  $P^{32}$  incorporation into DNA and ribonucleic acid (RNA) of human carcinoma of the cervix (255) and rat thymus (256) was decreased. Payne *et al.* (193) found that cytoplasmic pentose nucleic acid of liver incorporated  $P^{32}$  faster after irradiation but incorporation into both nuclear and cytoplasmic DNA was depressed. Skipper & Mitchell (233) have further shown that  $C^{14}$  formate and  $C^{14}$  bicarbonate both enter visceral DNA and DNA purines after x-irradiation more slowly than con-

trols. It is notable that, while depression in DNA synthesis is occurring, no depression in protein synthesis has been detected. Holmes & Mee (122), using inorganic  $S^{35}$  and methionine labelled with  $S^{35}$ , found no depression of incorporation into proteins, at the same time 50 per cent depression of  $P^{32}$  uptake into DNA was occurring. Pelc & Howard (194), using a radioautograph technique, obtained the same result for nuclear proteins of *Vicia faba*. Hevesy & Dreyfus (118) and Payne *et al.* (193) found no decrease and, if anything, an increase in  $C^{14}$  uptake from acetate and formate respectively into tissue protein following radiation. There is likewise no depression of  $P^{32}$  incorporation into phospholipid (84, 255, 256). There was been reported a depression in the ability of cells to esterify phosphate, however, leading to speculation as to the possible significance of this for DNA synthesis (233, 256).

Estimates of changes in DNA content of irradiated nuclei have been made by several investigators on the basis of visual observations of staining behavior. A loss was reported in epidermal cells of the guinea pig (188) and in epithelium of the gastrointestinal tract of the rat (257). No change in amount of DNA following irradiation is reported in nuclei of the lens (214). A similar observation was made from quantitative cytochemical measurements of *Trillium* pollen-mother-cells (238). A quantitative decrease in methyl-green staining has been interpreted to mean a decrease in polymerization of irradiated nuclei of grasshopper embryos (111) but no change could be demonstrated in *Trillium* (182). Irradiated tongue epithelium nuclei show changes in staining reactions interpreted to mean that irradiation results in nucleic acid complexes of a "less-aggregated state than normal" (37).

A number of experimental observations on cells can best be considered as physiological end-results of the radiation action. The subject of skin erythema has been reviewed by Belisario (23). The action spectrum for ultraviolet induced erythema has been determined to have peaks at 297  $m\mu$  and 250  $m\mu$  with a low at 280  $m\mu$ . By removing layers of skin, the stratum corneum has been determined as the locale of action attributable to the 250  $m\mu$  peak while the 297  $m\mu$  reaction occurs beneath this layer (210).

The effect of x-rays on the hair cycle in young rats has been studied by Geary (96). He concludes that maximum sensitivity coincides with maximum activity of the follicle. The matrix cells of the follicle are very sensitive, but in order to produce permanent epilation, the resistant dermal papillae must be killed.

Studies of the action of ultraviolet light (31) and  $\beta$ -particles (95, 274) on nerve electrical properties have been made. Following little or no effect at small doses, there is in general a progressive destruction of the action potential marked by increased threshold, prolonged refractory period, and decreased amplitude. Nachmonsohn (182a) has reviewed the problem of permeability changes in nervous tissue following radiation. He calls attention to the similarity of effects to permeability studies in erythrocytes.

Sheppard & Stewart (229) have studied the red cell *in vitro* under x-rays and find that cells leak potassium and take up sodium long before the appearance of any osmotic changes, such as swelling or hemolysis. There was no measurable effect on the glycolytic metabolism of the cells or on their cholinesterase activity.

The action of radiation on capillary permeability has been recently reviewed by McCutcheon (157).

#### EFFECTS ON MICROORGANISMS

An end-result of radiation on cells which has been extensively studied in the history of radiobiology is lethality, especially in the case of microorganisms. The interpretation of survival curves of *E. coli* following x-irradiation in the light of recent advances in bacterial cytology has been considered by Norman & Greenfield (184) and Atwood & Stapleton (16). It is pointed out that unless there is some unsuspected interaction between nuclei in such multinucleate cells that causes a lethal in one nucleus to influence the viability in another, it is difficult to explain the exponential survival curves obtained with x-rays either on the basis of recessive or dominant lethal mutations. Magni (164) has found a linear relationship between the cell volume and x-ray sensitivity of *E. coli*. A study of the inactivation of *Bacillus subtilis* spores as a function of electron energy for very low-energy electrons has been made by Davis & Hutchinson (64). They arrive at a figure of 500 Å for the maximum thickness of the inert surface layer of the dried spores since electrons with maximum ranges below this value leave a residual group of spores which cannot be inactivated. Their interesting survival curves are still awaiting interpretation. Heinmets & Taylor (112) have exposed *E. coli* to electrical discharge in vacuum and observed inactivation which is not photoreactivable with visible light. They attribute this to ionizing photons from the vacuum ultraviolet region of the spectrum (3–200 mμ).

Photosensitization, the process by which light induces reactions in biological systems which are exposed to dye molecules, has been studied for *E. coli* with methylene blue by Heinmets, Vinegar & Taylor (113). Based on studies in the frozen state, they attribute the primary step in the reaction to an excitation in a bacterium-dye complex as opposed to absorption of light in a free dye molecule leading to reactions attacking the bacterium. Calcutt (39) has shown that there is an effect of light on the bacterium, in such cases, independent of its action on the dye or dye-bacterium complex. By preirradiating *Paramecia* before exposing them to dye, he was able to enhance the subsequent photosensitization.

A comparison of the action of ultraviolet light on the lethality and the virulence of *Bacillus cereus* for *Bombyx mori* larvae has been made by Vago & Busnel (264). The loss of virulence occurs at lower doses than colony-forming ability.

That cultural conditions to which irradiated bacteria are subjected fol-

lowing irradiation can greatly affect the survival data in terms of colony-formation has been emphasized in the experiments of Engelhard & Houtermans (74) and Stein & Harm (110, 247). The latter authors find a markedly greater survival of organisms following ultraviolet irradiation if the cultures are incubated at 44.5°C. as compared to 37°C. A similar situation occurs in unirradiated cultures and the authors point out the similarities in behavior of ultraviolet inactivated organisms and these spontaneously "inactive" bacteria which can apparently be activated by heat.

Work on the chemical modification of radiation effects in microorganisms and the role played by dissolved oxygen in cell water has been discussed by Hollaender (120) and Latarjet (147). Hollaender has grouped the agents which protect bacteria into four categories (121). First are compounds with sulphhydryl groups such as cysteine; secondly, strong reducing compounds such as  $\text{Na}_2\text{S}_2\text{O}_4$ ; thirdly, such as compounds as methanol which protect in high concentrations or at low concentrations after a short pre-incubation period; lastly, compounds such as succinate which require long pre-incubations. The second (36) and fourth of these categories (245) have been the subject of recent papers. The strong reducing compounds lower molecular oxygen concentration by direct chemical action, whereas succinate and formate are visualized as becoming substrate for oxidative metabolism in the cells and thereby reducing molecular oxygen in the cells.

Mefferd & Matney (174) have found that pretreatment of *E. coli* with carbon monoxide can reduce the effect of ultraviolet irradiation on aerobic cultures, but can not further enhance the protection afforded by anaerobiosis. Moos (179) has shown the reduced sensitivity of bacteria in the dry or frozen state. However, the sensitivity when dried out of distilled water is greater than that in frozen broth which is in turn greater than in dried broth.

In many cases of radiation damage, hydrogen peroxide has been considered not to be the main agent involved in damage since its concentration in irradiated solutions is too low. However, Kimball & Gaither (133) find that this agent contributes two-thirds to three-quarters of the nongenetic death and division delay in *Paramecium*. No genetic effects were detected and the authors feel that the high concentrations of catalase within the organisms protect the deepseated genetic elements.

A restorative action of catalase on the ultraviolet survival of bacteria in the presence of small amounts of visible light has been the subject of work by Latarjet (146), Latarjet & Caldas (148), and Miletic & Morenne (177). The action is interpreted as a peroxidatic action of the enzyme which acts on some slowly decaying active radiation product. The ability to be restored with catalase is linked to the phenomenon of lysogenesis and can only be demonstrated in lysogenic strains.

Photoreactivation, the process whereby an exposure to visible light in the blue-purple part of the spectrum is capable of counteracting the effect of a preceding exposure to ultraviolet light, has been shown to be a general biological phenomenon found in plants, animals, bacteria, and viruses for a



number of different biological properties. Bawden *et al.* (22) found that damage to the leaves of *Phaseolus vulgaris* resulting in cell death and inability to support virus growth could be prevented by following ultraviolet exposure with visible light. Salamander larvae, although completely killed by large doses of ultraviolet, do show photoreactivation at smaller doses (29). Visible light practically eliminated mutations induced in *Drosophila* by irradiating polar caps with ultraviolet (11). Giese *et al.* (97) point out that division rate probably determines the rate of decay of the ability to be photoreactivated, since in *Paramecium* there is actually some increase in photoreactivability with increasing time intervals between the ultraviolet and visible light exposures. This is only true if the reactivation is carried out before the first division following the ultraviolet treatment.

In microorganisms, photoreactivation of induced lag in growth (22a) and its independence of the ploidy of the organism (266) have been demonstrated. Magni (165) claims that photoreactivation occurs only in the long snake-like forms seen in *E. coli* cultures after irradiation.

Photoreactivation has been demonstrated for tobacco necrosis virus, but not for tobacco mosaic virus by Bawden *et al.* (22). Hill & Rossi (119) found no photoreactivation in *E. coli* bacteriophage T1 when ultraviolet irradiation was performed on phage that had been deposited on coverslips by spraying it from broth or ammonium acetate solutions and then allowing it to dry.

#### CYTOLOGICAL EFFECTS

The cytological aspects of radiation damage have been reviewed by a number of authors (65, 78, 79, 125, 201, 236, 240, 277). In addition to these reviews, several comparisons of the cytological effects of ionizing radiations with the effects produced by the so-called "radiomimetic" chemicals have appeared (2, 32, 67, 140, 187, 249).

Biochemical and physiological effects at the cellular level have already been discussed above. The following paragraphs deal mainly with papers concerned with morphological changes induced in cells or cellular components. However, it should be understood that many of these articles consider both the physiological and structural deviations from normal. Papers dealing mainly with histopathology are covered elsewhere in this volume (93).

*Cytoplasmic effects.*—Compared to nuclear damage, relatively few effects on cytoplasmic structures have been reported. Vacuoles sometimes appear (173, 209), and the cytoplasm becomes less dense (160) and may change in degree of basophilia. High dosage irradiation of *Endomyces magnusii* has revealed a pronounced contraction of the protoplasm, changes in cell turgor, swelling of the terminal section of the mycelium, and various reorganizations of the vacuoles, all of which are temporary and reversible. These are followed by a general gelatinization of the protoplast and have frequently been overlooked [Medvedeva *et al.* (173)]. In the growing point of barley plants containing P<sup>32</sup>, the cells are enlarged and the cells walls are unusually thick.



The whole region looked abnormally mature (160). A similar effect on the degree of differentiation is also reported by Glucksmann (100) following irradiation of both normal and malignant human tissue. Disruption of the mitochondria of yeast by ultraviolet irradiation (216) and clumping of mitochondria in x-rayed grasshopper eggs (254) has been described. A peculiar "bubbling" in irradiated cytoplasm of amphibian heart cells has been observed in live preparations (279). The significance of this phenomenon is unknown.

*Effects on the nucleus.*—The nucleus of the cell has long been known to be more sensitive to radiation damage than the cytoplasm or cell wall. This is reflected in the large number of papers dealing with nuclear effects relative to those describing cytoplasmic or nonnuclear damage. Nondividing cells do not usually show morphological changes following low or medium dosages but show a number of effects after larger exposures. Simple swelling or increase in nuclear volume has been described in hamster thymus and bone marrow (after 100,000 r) (211) and in ovarian follicles of the mouse from the internal  $\beta$ -radiation of  $P^{32}$  (186). In the latter case, cell volume is also increased and the frequency of such "blown-up" cells along with measurement of apparent diameters is thought to be useful as a quantitative measure of early irradiation effect. The ratio of cytoplasmic to nuclear areas has been studied by Johnston (127) in carcinomas. He found that 19 per cent of the cells in the control samples had ratios less than 3.5 while in irradiated samples 32 per cent of the cells had ratios less than 3.5. These data are a further indication that normal volume relationships between nucleus and cytoplasm are disturbed following exposure to ionizing radiation. Continuous local irradiation (from  $P^{32}$ ) of the tongues of mice has produced large atypical nuclei containing "clumps of chromatin" [Burstone (37)] and Brues & Reitz (35) have reported enlarged or polyploid nuclei in liver cells following repeated or chronic irradiation. Variation in nuclear volumes of the nonirradiated cortex of the suprarenal gland associated with irradiation of remote portions of the body (hypophysis, testis, or thigh) is also described (144). Radiosensitive cells of mice, rats, and dogs frequently show intranuclear vacuoles shortly after exposure to ionizing radiation (209, 265). Nuclear membranes may also show an irregular or wrinkled appearance. In some cases the nucleoli seem to act as foci of vacuole formation. The vacuoles may become large enough to cause stretching and even rupture of the nuclear membrane leading to cell destruction (265).

Other morphological changes described in nuclei following x-irradiation include clumping of chromatin, pyknosis, and karyorrhexis (nuclear fragmentation). Since these are well known phenomena specific references are omitted except for the work of Tahmisian & Adamson (254) who made a detailed study of pyknosis in the living cell by phase contrast microscopy. They found the onset of the pyknosis could be delayed as long as six months by keeping irradiated grasshopper embryos at 0°C. They also noted that a drop in viscosity (based on observations on Brownian movement) occurred

at the time of pyknosis. Ultraviolet light has also been shown to cause changes in the structure of the macronucleus of *Paramecium* (132) and breakdown of the nucleolus of grasshopper neuroblasts (45). Both of these effects show the photoreactivation phenomenon.

*Effects on nuclear and cell division.*—Probably the most familiar effect of radiation on cell division is chromosome and nuclear fragmentation. However a number of other effects have been described or reinvestigated, and these will be reviewed briefly.

Studies of the interference with cell division of microorganisms has led to some rather interesting results. Barron (21) found that small doses of x-rays, which produced an increase in respiration of *Arbacia* eggs, were sufficient to cause delay in cleavage to the two cell stage. Eventually, however, the eggs reached the same per cent of cell division as was found in the controls, which is to be expected where a dosage well below the sublethal dose is used. Daniels (62) has also noted delay in division of the amoeba, *Pelomyxa carolinensis*, following exposures of 60,000 to 100,000 r. With dosages above 70,000 r the numbers of daughters produced per plasmotomy decreased. The delay in division could be largely prevented by fusing nonirradiated halves to irradiated halves. These results indicate that some nonirradiated component of the cytoplasm somehow has the ability to promote recovery from x-ray injury. This experiment should be compared with the protective effect observed in irradiated mice following injection of bone marrow suspensions [Lorenz *et al.* (151)]. Unfortunately neither of these investigators has yet been able to identify the substance (or substances) responsible for the modifying effect.

Mitotic inhibition following exposure to radiation has been reviewed by Hevesy (117). Helmke (114) observed the effect of 300 and 500 r of daily doses of Chaoul radiation on prickle cell and basal-cell human skin carcinomas. A gradual drop in the number of mitoses was observed in most of the cases and in a few delayed mitotic waves appeared. The mitotic index of mouse epidermis was also studied by Smith (235) following x-rays with and without administration of thyroid hormone. The latter alone caused an increase in mitotic rate without radiation but had no effect on the reduced mitotic index following whole body x-irradiation.

Koller & Casarini (140) compared the effects of x-rays and nitrogen mustard in femoral bone marrow and implanted Walker carcinoma of the rat. Chromosome damage and numbers of dividing cells were compared at various times. They conclude that the "primary basic reactions initiated by these agents are fundamentally different," although many of the effects are superficially similar.

Brues & Reitz (35) found that the amount of  $\beta$ -radiation required to reduce liver mitosis by one-half is of the order of 1 rep/hr. over a 48 hr. period. They also suggest radiation death in higher animals and the induction of regression of tumors by radiation may depend primarily upon chromosome damage. Histological studies following irradiation of the hibernating marmot

also led Brace (33) to the conclusion that "interference with cell division is an important factor in the lethal process."

The relative numbers of the different mitotic stages in chick heart fibroblast cultures has been used by Gartner (94) as a measure of the effectiveness of 6 Mev electrons and 90 kv. x-rays. The study showed that 500 r of fast electrons was about 50 per cent as effective as 500 r of x-rays. A similar comparison of the effects of 4 Mev electrons and 180 kv. x-rays on mitotic index of *Vicia faba equina* also showed the fast electrons to be less effective (221). Both these cases can best be explained on the basis of differences in ion density produced by the two types of radiation (see also p. 359).

Mitotic or meiotic inhibition has also been studied in several other plants. Kurabayashi (141) found that the percentage of cells showing chromosome aberrations at various times after irradiation was temperature dependent. The lower the temperature the longer it took for the aberrations to reach a maximum. A relationship between the average amount of chromosome fragmentation per cell and the degree of inhibition (i.e., increase in time required to pass from one stage to another) has been shown in *Trillium* cells even when all chromosome fragments are present in the damaged nuclei (238). Relative numbers of mitotic divisions in the root meristem of wheat seedlings was plotted after 24, 48, and 72 hr. exposures to aqueous solutions of  $P^{32}$  (262). At low levels a small increase in the number of mitoses were noted but from 0.5  $\mu$ c. per ml. up, there was a sharp decline. At the 20  $\mu$ c. per ml. level the percentage of mitosis fell to 14 per cent of the control values at 24 hr. and 0 per cent at 72 hr. The effect of  $P^{32}$  on growth of root also has been investigated by Russell & Martin (213). Reduced growth is attributed, in part, to chromosomal damage and, in part, to physiological disturbances. The relationship between growth inhibition of roots and mitotic inhibition also has been studied in Mung beans by Quastler, Schertiger & Stewart (198). They concluded that the growth inhibition is not the direct result of the radiation effects on mitosis but that the "effect on growth must affect some mechanism which operates on the cell after it has been formed; it must interfere with the process of elongation." They also suggest that an effect on auxin may be related to the growth inhibition. Such an effect has been demonstrated by Gordon & Weber (101).

In addition to mitotic inhibition several other abnormalities or disturbances frequently result from irradiation. Giant or polyploid nuclei are frequently observed (35, 58, 178, 214, 242) which presumably result either from spindle inhibition or fusion of daughter nuclei to form a single 4n nucleus. Irradiated amphibian cells also have revealed inhibition of anaphase movement, inhibition of metaphase configuration following prophase irradiation, inhibition of cytoplasmic constriction, unequal distribution of chromosomes to daughter nuclei, and interference with reconstruction of daughter nuclei [Zirkle & Bloom (279)].

Bilobed nuclei (124) and bi- or multinucleate cells (150, 209, 214) as well as cells with small accessory nuclei (micronuclei) are commonly ob-

served (178, 241, 279). The latter usually result from lagging acentric fragments which in most cases degenerate in the cytoplasm and leave a chromatin deficient nucleus (which can be assumed to be also genetically deficient).

*Effect on chromosomes.*—Chromosome breakage, recombination of broken ends, the relationship between breakage and gene mutation as well as considerations of various factors influencing these processes have been considered in a long list of papers. Reviews covering one or more of these topics have appeared by Darlington (63), Read (201), Smith (234), Sparrow (236), Sparrow & Rubin (240), Tolbert & Pearson (260), and Ulrich (263), as well as a book by Grobman (107) emphasizing the genetic effects of ionizing radiation.

The distribution of radiation-induced chromosome breaks has been studied by Morris (180) in *Zea mays*, by Deufel (67) in *Vicia faba*, and by Gottschalk (102) in *Solanum lycopersicum*. In *Zea*, thermal neutron-induced breaks showed a statistically random distribution among chromosomes, chromosomes arms, and sections of arms (180). In *Vicia* root tip cells there was a random distribution of breaks between the M- and m-chromosomes but in the satellite chromosomes there was an excess of breakage in the region proximal to the centromere, and in the SAT-zone. The distribution of breaks induced by treatment with urethan was somewhat different from that produced by x-rays. In *S. lycopersicum*, cells irradiated at premeiotic interphase and analyzed at pachytene also showed an excess of breaks (73 to 82 per cent) localized near the centromere. This may be associated with the fact that proximal regions of *S. lycopersicum* chromosomes are largely heterochromatic. However, chemically induced breaks (ethylurethan and aluminum chloride) did not show any excess in the heterochromatic region. These papers can be interpreted to mean that somewhat different mechanisms of breakage are involved in radiation-induced than in chemically-induced chromosome breakage [see reviews by Auerbach (17); D'Amato (61); Levan (149)]. From x-ray experiments with *Drosophila*, Luning (153) also has concluded that certain regions of the chromosomes behave differently than others with respect to irradiation. He proposes two types of chromosomal material: (a) invariable and (b) variable. Hits in the former may produce breaks or other changes, including intragenic mutations. Hits in the variable elements produce breaks but seem to produce mutations only as a result of rearrangement i.e., intergenic mutations.

The effect of separating two equal doses of x-rays by a variable time interval has been reinvestigated by Lane (143). Using *Tradescantia* pollen he found that the break frequency decreased as the time between fractions increased up to 4 hr. but that after 4 hr. the break frequency gradually increased until by 8 hr. it approached that of a continuous dose. On the basis of these results he rejects the idea that most breakage and reunion must occur in a matter of a few minutes. If confirmed, this would be a severe blow to accepted concepts concerning the nature of breakage and reunion as now accepted [Catcheside (47)]. However, further careful experiments of

Sax & Luippold (217), DeSerres & Giles (66), and Steffensen & Arnason (246) have failed to confirm Lane's findings. Some support for Lane's contention is given in the work of Caldecott & Smith (40) who found evidence of some delayed reunion in barley.

Cells have been irradiated in various premeiotic stages or in meiosis or microsporogenesis in *Trillium* (172, 236 to 239), *Hyacinthus* (178), *Oenothera* (170), *Vicia* (169), *Gesonia* (200), and the induced chromosome or chromatid breakage and reunion have been studied. Matsuura & Haga (172) found a close relationship between chromosome length in *Trillium* and the frequency of breakage, i.e., the long A chromosome showed about twice as many breaks as the short E chromosome. They also claim that certain breaks can remain open and conversely that a normal chromosome end can unite with a free broken end. This latter is in disagreement with the established concept that only broken ends can reunite with each other (and not with normal ends). Also working with *Trillium*, Sparrow & Maldawer (237) reported that the amount of detectable rejoining of broken ends varies with the stage irradiated, being higher at a stage of low break-sensitivity (early postmeiotic interphase) than at a stage of high breakage (first meiotic metaphase). In contrast to these results, however, Ray-Chaudhuri & Sarkar (200) found that the number of bridges at first meiotic anaphase did not vary significantly following fixation 10 to 108 hr. after irradiation. They also found that the number of bridges is directly proportional to dosage and does not increase as the square of the dose, as would be expected if they resulted from two independent breaks. They, therefore, conclude the bridges result from "one or more breaks caused by a single ionization or activation, or occurring in the course of a single ionizing track." Marquardt (170) compared the effects of x-rays and zephiran on meiosis of *Oenothera hookeri* and found dechromatinization to result from both. Following the detergent he found mostly chromatid translocations whereas those produced by the radiation were mostly chromosomal. Irradiation of *Vicia faba* has shown a decrease in chiasmata frequency six days after exposure (169). This is of special interest since it indicates an interference with the mechanism of genetic crossing over.

Several studies have been made of the frequency and behavior of aberrations induced in various somatic cells or tissues in both plants and animals. Arnason *et al.* (14), treated seedlings of wheat and barley with  $P^{32}$  and later found groups or blocks of cells showing aberrations at meiosis. Mutant plants obtained in later generations also showed evidence of chromosome aberration. Gene and chromosomal damage inflicted in plants by neutrons, x-rays,  $P^{32}$ ,  $S^{35}$ , and radon have been studied for some time by a group of Swedish investigators (71, 72, 73, 109, 159). Many interesting results have been obtained by the investigators but only a few can be considered here. As would be expected neutrons and  $\alpha$ -particles are more effective than x or  $\beta$ -rays in causing chromosomal damage (72, 159), but cells damaged by neutrons are eliminated (presumably by cell death) less effectively than those



damaged by x-rays. Chromosomal aberrations induced by x-ray and thermal neutron-irradiated seeds of barley have been studied by Caldecott, Frolik & Morris (42). They found that a similar amount of chromosomal aberration produced more severe seedling injury following x-ray than following neutron treatment and concluded that "apparently x-rays have proportionately more effect on the extrachromosomal elements of the cell than do thermal neutrons." The frequency of various types of aberrations (mostly translocations) induced in dormant seeds has been studied by Caldecott & Smith (40) in barley, and by Matsumura (171) and Yamashita (275) in wheat (*Triticum monococcum* and *T. Aegilopoides*). Reciprocal translocations were common in all three studies. In barley, Caldecott & Smith (40) examined 3509 spikes and found 423 which showed evidence of reciprocal translocations (rings of four or more chromosomes at first meiotic metaphase). Their evidence "suggests that all the microsporocytes in a barley spike usually arise from a single cell in the dormant embryo." If true, this might account for the large number of translocations which persist through a long series of somatic divisions. These authors also point out that in their material, fusion of sister chromatids or pairs of sister chromatids did not often occur but go on to suggest that "it seems that the centromere plays an important part in the union of broken ends of chromosome fragments." In the opinion of the present reviewers, further data in support of this conclusion is desirable.

It has recently been demonstrated that ultraviolet light radiation can produce chromosome breakage (followed by restitution) in *Drosophila* [Faberge & Mohler (80)]. Previously it was considered that ultraviolet produced gene mutations but few or no breaks.

It is generally considered that dicentric chromosomes can exist for only a short time because of bridge formation at anaphase followed by breakage. However an exception to this rule has been reported by Sears & Camara (224) in common wheat. Its survival is apparently attributable to the fact that the second centromere is relatively weak and generally moves to the same pole as the primary centromere. Another interesting and unusual observation has been reported by Resende (206). He found that neutron treatment of root tip cells "causes extrusions from the resting nucleus which, once fragmented, separate from the latter, coexisting with it in the same cell."

An apparatus for the irradiation of localized parts of cells has been developed by Zirkle & Bloom (279). Their microbeam of protons can be limited to diameters as small as 2.5  $\mu$ . They found that even a few dozen protons, when delivered to the chromosomes, regularly produced abnormalities (mainly bridges) but that hundreds or thousands of protons delivered to nonchromosomal portions of the cell produced no apparent effect on the chromosomes. This new technique will undoubtedly prove to be a very valuable addition to the research equipment of the cellular radiobiologist.

The mechanism of radiation induced chromosome breakage, and the probable relationship of molecular damage to chromosome breakage is dis-



cussed by Sparrow, Moses & Dubow (238). They suggest that damage to the protein component is a prerequisite to chromosome breakage but do not exclude damage to other components from being involved.

In addition to chromosome breakage and mutation, ionizing radiation also has certain less well defined effects. It is well known that clumping of chromosomes, or chromatin, frequently occurs with concomitant sticky chromatin bridges at anaphase. In addition to these, two other effects have recently been described (238). These are a partial failure of chromosome spiralization in mitosis (35) and in meiosis (238) and an inhibition of chromonemal elongation which is normally associated with formation of the major spiral. Cytochemical measurements of DNA failed to show any significant difference between irradiated and control nuclei (238). An effect of irradiation on chromosome length has also been noted in *Vicia faba equina* (221). Other radiation effects on nuclear components are described on page 349.

#### FACTORS INFLUENCING RADIOSENSITIVITY OF CELLS

This topic has been reviewed recently by Cronkite & Brecher (57), Herve & Bacq (116), Patt (189, 190), Selle (225), Sparrow (236) and various authors at the Oberlin Symposium (183). It will be considered here as briefly as possible.

*Biological factors.*—Under this heading we shall consider only those factors which can be considered to be conditions or processes associated with the internal environment of the organism. Many examples in this category have been known for some time but only a few receiving special attention will be mentioned here.

Changes in radiosensitivity associated with the stage of cell division have been studied by Sparrow, Moses & Dubow (238) in *Trillium*. Late meiotic prophase (diplotene and diakinesis) and first meiotic metaphase are 50 to 60 times as sensitive to x-rays as early postmeiotic interphase. Sensitivity increases in later interphase. They point out an apparent inverse relationship between radiosensitivity and length of chromonemata and also that "diplotene, a high point on the sensitivity curve, is a stage when chromatids seem to be mutually repulsive. In contrast, at telophase (or early interphase), a stage of low sensitivity, the chromosomes show marked mutual attraction." They further suggest that these reactions may reflect changes in the electric charge on the chromosome surface which in turn may "have an effect on the initial reactions leading to chromosome breakage as well as on subsequent rejoining." In *Paris* (a close relative of *Trillium*), prophase has been found to be the most sensitive in somatic cells in the young ovary (142). In line with these observations are the results of Russell & Michelini (212) on corn seedlings and on Schjeide & Allen (220) on tadpoles indicating that the amount of radiation damage is correlated with the percentage of cells involved in mitosis at the time of exposure. Rearrangements in  $F_1$  progeny of x-rayed males of *Drosophila hydei* were studied by Fiala & Neubert (83). They found that

4000 r produced 27.8 per cent, 0.7 per cent, and 45 per cent rearrangements, respectively, in sperm, spermatocytes, and unfertilized eggs. They also found that aberrations induced in immature stages (larvae and pupae) could appear in the sex cells of mature flies. Changes in radiosensitivity with age of pupa (92), stage of spermiogenesis, and age of males has also been shown in *Drosophila* [Luning (152)]. Difference in sensitivity between somatic and meiotic cells of *Tradescantia* were observed following exposure to chronic  $\gamma$  radiation. Based on the amount of chromosome fragments, meiotic cells are about 10 times as sensitive as somatic tissue [Sparrow & Singleton (241)]. This is in line with the generally recognized high radiosensitivity of the meiotic cells in both plants and animals (7, 86, 87, 238). Unfortunately the reason for the high sensitivity of such cells is not known, nor is there any adequate explanation for the unusually high sensitivity of certain other cells, such as lymphocytes, which appear to be the most sensitive cells of the body (261).

Many attempts have been made to correlate sensitivity with the physiological activity of the cell or tissue [See reviews by Brues & Reitz (35), Hevesy (117), and Patt (190)]. Hibernating animals (33), or animals kept at low temperatures (8, 254) following irradiation, are relatively slow in showing the radiation damage. Low temperature, however, does not always appear to decrease the radiation sensitivity. Kurabayashi (142) found a greater incidence of chromosome aberrations at 0° and 10° C than at 20°C in x-ray treated plants of *Paris tetraphylla*, and Latarjet (147) found that a yeast (*S. ellipioideus*) showed less injury when kept at 5°C but that the low temperature had no effect on injury to a bacterium (*B. dysenteriae*).

Several authors have looked for a relationship between the amount of DNA per cell and the radiosensitivity. In *Trillium* microsporogenesis stages of increasing sensitivity (to chromosome fragmentation) are stages during which DNA content is also increasing. However, during the period when sensitivity falls, no change in DNA was detected (238). Cornil & Stahl (55, 56) have also made cytochemical measurements of DNA and RNA<sup>2</sup> on lymphosarcoma and orthoplastic epitheliomas. They conclude that the radiosensitivity of a cell is proportional to its content of nucleoproteins, and also that the ratio of DNA/RNA can be used as an index of radiosensitivity. A similar suggestion is offered by Brues & Reitz (35). Mallet & Pinsky-Moore (166, 167) have also made photometric determinations of DNA in cancer cells and state that DNA content can be used to predict the radiosensitivity.

The above relationship seems like a reasonable one but one that will not be expected to hold in cases of polyploidy. Polyploid nuclei are known to contain proportionately more DNA than diploid cells [Swift (251); Moses *et al.* (181)] but several authors have shown a decrease in sensitivity to be associated with increasing polyploidy in yeast (147, 215, 259, 266), in *Habrobracon* (50), in rat tumor (58), and in plants (139, 241). A comparison, of chromosomal damage in 2n and 4n *Tradescantia*, by Bishop (27) indicates that the breakage is proportional to the chromosome number, i.e., that the number of breaks per chromosome is not dependent upon chromosome num-

ber. It, therefore, seems highly probable that the greater tolerance of polyploids in general must be based on the fact that damage to one chromosome set will be masked by one or more of the remaining genomes. An exception to this has recently been reported by Clark & Mitchell (51). They found haploid *Habrobracon* pupae to be more resistant during cleavage or, if irradiated immediately after cleavage, of equal tolerance to the diploid.

Water content has long been known to have an effect on radiosensitivity. Confirming data have been obtained with *Aspergillus terreus* spores [Stapleton & Hollaender (243)], pollen of petunia [McQuade (162)], and with seeds of barley (72).

*Chemical modification of cellular radiosensitivity.*—A fairly extensive literature now exists on chemical modification of radiation damage. This is an important field of investigation, but because of space limitations only those papers which clearly fall within the term "cellular radiobiology" will be reviewed. For protection at the macroscopic level the reader is referred to the papers of Cronkite & Brecher (57), Herve & Bacq (116), Patt (189, 190, 192), and Hempelmann (115). (Protective studies dealing primarily with microorganisms are reviewed on p. 346).

Investigations on the protective effect of reduced oxygen tension have been continued in several laboratories. In *Drosophila* Baker & Edington (19) found a reduction of about 75 and 50 per cent, respectively, in translocations and sex-linked recessive lethals by irradiation in nitrogen. Schwartz (223) irradiated maize pollen and found anoxia to give protection against interstitial and terminal deletions. He states that "chromosomes broken in the absence of oxygen are more capable of rejoining than chromosomes broken in the presence of oxygen." The effect of low oxygen tension on x-ray induced chromosome breakage and reunion in *Tradescantia* has also been studied by Giles (98) and by Riley *et al.* (208). Giles is of the opinion that the increased sensitivity in the presence of  $O_2$  is attributable to a substance produced by the radiodecomposition of water and suggests that the substance may be  $H_2O_2$ . Giles, and Riley *et al.*, in contrast to the conclusion of Schwartz, favor the idea that the oxygen acts on the breakage process rather than modifying the recovery or reunion process. Giles *et al.* (99) have extended the study of oxygen effect to the aberrations produced by fast neutrons. They report the effect to fall between that found with x-rays and  $\alpha$ -particles. The relationship between aberration frequency and dosage is linear for all types of aberrations whether the neutron treatment was made in the presence or absence of oxygen. This observation is taken as further evidence for localization of radiation effects to the immediate vicinity of particle tracks.

In connection with the protection effect of low oxygen tension, the work of Conger & Fairchild (53) should be mentioned. They found that pure oxygen without any radiation could induce chromosome breakage in pollen of *Tradescantia*. Further study along their lines would be highly desirable.

The effect of various oxygen pressures on growth of *Vicia* roots has been reported in a series of papers by Read (201 to 205). Since cytological an-

alyses of radiation damage were not made, these papers are being mentioned mainly because their discussions and explanations are primarily at the cytological level. Read's articles should be read carefully by all concerned with the mechanism of the oxygen effect. A partial reduction of growth inhibition in x-rayed pea seedling roots has been obtained by treatment after irradiation with  $10^{-9}M$  indol acetic acid (IAA) or 0.2 per cent IAA<sup>2</sup> in lanolin paste (175). It would appear to be of considerable interest to test whether IAA would have any effect on nuclear or chromosomal damage. Apparently this has not yet been determined. However, it is known that irradiation can reduce the concentration of IAA in certain plants (101).

King, Schneiderman & Sax (134) have investigated the effect of CO and O<sub>2</sub> alone and in combination on chromosome fragmentation in *Tradescantia*. The increase in aberration frequency depends upon length of exposure to CO prior to irradiation, with a maximum at one hour prior exposure. This increase is almost completely prevented if O<sub>2</sub> is also present in high concentration. The authors suggest that the CO exerts its action on the breakage process rather than on the recovery process. These very interesting results are explained as follows:

We believe that CO affects a heavy-metal-containing enzyme in the microspores, probably cytochrome oxidase, in the cytoplasm, nucleus, or both. Furthermore, we suggest that when cytochrome oxidase is inhibited by CO, the flavoproteins act in a greater measure than usual as terminal oxidases, producing large amounts of H<sub>2</sub>O<sub>2</sub>. This H<sub>2</sub>O<sub>2</sub> sensitizes the chromosomes to irradiation. We believe that oxygen, on the other hand, affects the flavoproteins in the microspores: low oxygen tensions decrease their activity as terminal oxidases and this reduces the production of H<sub>2</sub>O<sub>2</sub>; high oxygen tensions increase their activity, and this increases the production of H<sub>2</sub>O<sub>2</sub>. Oxygen when applied simultaneously with CO almost completely reverses the effect of CO on chromosome aberrations presumably by reversing the CO-inhibition of cytochrome oxidase.

King & Schneiderman (135) also have found that a concentration of carbon dioxide as low as 0.5 per cent of an atmosphere causes an increase in radiation induced chromosomal aberrations in *Tradescantia*. The aberration frequency increases with increasing concentrations of carbon dioxide up to 1.33 atmospheres of carbon dioxide (added to one atmosphere of air). No explanation for the effect is offered.

A protective effect of glutathione against radiation-induced chromosome breakage in root tip cells of *Tradescantia* has been reported by Mikaelson (176). Devik has examined the chromosomes of bone marrow cells in mice first treated with glutathione, thiocoline, thiourea, ascorbic acid, methylene blue and vitamin B<sub>12</sub> and then exposed to 200 r of whole body x-irradiation (68). He found no significant decrease in chromosomal aberration following any of these pretreatments although hypoxia did show a reduction in frequency of aberrations. He, therefore, concluded that the effect of the protective agents which showed no change in chromosomal injury must be a cytoplasmic one. However, in view of Mikaelson's positive results (see above)

this conclusion must be treated with some skepticism pending further investigations.

Patt *et al.* (191) have observed the protective effect of cysteine, on *in vitro* x-irradiated thymocytes. The effect is strongly dependent on the relation between the time cystine is added and the time of irradiation, even though the concentration in the cells may be the same at the time of exposure. It has been pointed out by Whitehead (273) that care must be taken in studying protection against ultraviolet radiation to rule out absorption by the protector itself.

*Physical factors modifying radiosensitivity.*—A number of papers have already been mentioned above in which a physical factor, e.g., temperature (8, 142, 147, 225, 254) has a modifying effect on radiosensitivity. In addition to these, Caldecott & Smith (41) have studied the influence of heat treatments on the injury and cytogenetic effects of x-rays on barley. They found that appropriate treatments did influence the seedling height, and both chromosomal aberrations and mutations in x-rayed material. However, since the heat decreased the injury and aberrations and increased the frequency of mutations it was concluded that these three are not necessarily correlated effects of x-rays. In contrast to these results Alicata (7) found no differences in the results of irradiating *Trichinella* larvae at 0° and 24°C.

The effect of infrared pre- and posttreatment on the cytogenetic effects of ultraviolet and ionizing radiation has been known for some time. Additional data on chromosome aberrations in *Tradescantia* have shown that (a) the response to increased dosage of infrared is nonlinear; (b) there is a threshold value and a definite maximum; (c) posttreatment with a lowered intensity of infrared gives a reduction in aberrations but; (d) when given as a pretreatment a lowered intensity of infrared has no effect on the number of aberrations recovered [Yost (276)]. The "activated state" hypothesis previously proposed by Swanson & Yost (250) is supported by the additional data presented by Yost (276).

The comparative efficiency of betatron  $\gamma$ -rays and ordinary x-rays has been determined to be 0.83 for transplantable mouse tumors by Ting & Johns (258). Similar results were found for *Drosophila* eggs of various ages according to Schinz *et al.* (219). It also has been shown that  $\alpha$ -rays are more efficient than x-rays in inactivating spores of *Aspergillus terreus* (244). The effect of ion density on chromosome damage has been studied by Schermund & Heinrich (221) in *Vicia*. They found 4 Mev electrons to be less effective than 180 kv. x-rays on the basis of change in mitotic rate, shortening of chromosomes, and on the production of fragments and bridges. Further consideration of the biological significance of linear ion density is available in the reviews of Gray (104, 105, 106), Read (201), Ulrich (263), and in the "Symposium on Radiobiology" (183).

We have already discussed certain experiments designed to show the effects of modifying factors on survival after radiation. Zirkle (278) has analyzed rather thoroughly the use of survival curves, and of modifying factors

thereon, to interpret the nature of the events occurring in the cell following radiation. His considerations emphasize that on the basis of present data it is difficult to take either one of the extreme positions represented, on the one hand, by those who would have all radiation damage occurring by energy liberated within and destroying critical large molecules in the cell and, on the other hand, by those who would consider cell damage to result from secondarily mediated chemical reactions attributable to active solvent molecules within the cell. Just as it is conceivable that use of physical modifying factors such as changing ion density may be explained through differences in production and recombination of active solvent radicals, so may chemical modifying procedures possibly involve changes in the structural stability of macromolecules which change their sensitivity to absorbed radiation energy. Future research we hope will define the proper proportion of these so-called "direct" and "indirect" mechanisms. In experiments on germination and growth delay in seed and pollen, Rajewsky (199) has attempted to estimate this proportion by eliminating diffusion processes by irradiating at liquid air temperature. He interprets his data to indicate that diffusion processes account for 80 per cent of the effect at room temperature. Pollard (196) estimates the direct effect to account for approximately half the total effect on cells with  $\gamma$ -rays and x-rays. With more densely ionizing irradiation, such as neutrons, he considers the action to be 90 per cent direct.



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# PRACTICAL ASPECTS OF RADIATION INJURY<sup>1</sup>

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It is the purpose of this review to describe some of the manifold reactions of the human body to ionizing radiations. Beginning with high doses, the first part of the paper deals with the description of acute radiation injury in man. Following this a brief appraisal is made of the possible lines of therapeutic alleviation which are suggested by current animal experimentation. The last part of the paper affords a transition from high to subacute doses and describes late tissue reactions which arise at various dosage levels.

## ACUTE RADIATION INJURY IN MAN

Acute radiation injuries occurring in the field of nuclear science are most likely to be the result of inadvertent exposure to ionizing radiations from high-energy accelerators, from radioactive materials, or from nuclear fission reactors. Fortunately, such accidents are uncommon, but they have occurred often enough to make the resulting injuries a matter of interest to radiation workers.

The character of radiation injuries as they occur in man has been established and will be presented in a general way. In order to explain the clinical pattern of the injuries, it is first necessary to consider briefly a few fundamental facts about the nature of radiation injury. Injury to and death of individual cells within the tissues occurring on a microscopic scale are responsible for the gross reaction and the illness resulting from such exposure. Therefore, for an understanding of the injuries, the radiation reaction must be viewed at the cellular level. Much information about the response of cells has been gained from experimentation on animals and simple organisms. Sufficient knowledge, however, has been required by studying injured persons to make it clear that a similar type of response to radiation occurs in man.

The injury and death of cells exposed to ionizing radiation are unique in many respects. They are described in detail in Lea's book *Actions of Radiations on Living Cells* (1) in the recent Oberlin *Symposium on Radiobiology* (2), as well as in the Sparrow & Forro review in this volume (page 339).

In the following, consideration is given to actual injuries which have occurred as a result of high radiation doses during recent years. The illness of

<sup>1</sup> The survey of the literature pertaining to this review was concluded in February, 1953.

the Japanese exposed to the nuclear explosions and that of persons involved in the two nuclear accidents at the Los Alamos Scientific Laboratory provide us with excellent, although tragic, examples of the acute radiation syndrome. This name, "the acute radiation syndrome," is applied to the sickness produced by exposure of the entire body or a large part of the body to penetrating radiation. In contrast to this form of radiation injury, the hand injuries of four persons who handled radioactive materials at the 1948 Eniwetok tests are examples of acute superficial injuries produced by  $\beta$ -rays. The sole instance of the acute radiation injury produced by internally deposited radioactive materials is found in the history of a girl who committed suicide by drinking a solution of thorium.

*Japanese cases.*—The study of the Japanese exposed to the nuclear explosions at Hiroshima and Nagasaki provides us with a rich source of data on the effects in man of a single exposure of the entire body to penetrating radiation. There are limitations, of course, to an investigation of this type begun under the catastrophic conditions produced by the bombings. They include the lack of good radiation measurements in the injured persons and complications of the radiation injuries introduced by simultaneous burns and mechanical wounds. Poor personal hygiene and lack of medical care confuse the medical picture of the illness. Nevertheless, a vast amount of data was amassed by the Japanese physicians even under the conditions existing immediately after the explosion. Since then, the Joint Commission to Investigate the Effects of the Atomic Bomb, collaborating with the Japanese authorities, and, more recently, the Atomic Bomb Casualty Commission have done an excellent job of obtaining medical data. They have also carefully reconstructed the exposure conditions of persons who survived the immediate effects of the explosion and are able to estimate the relative exposures with surprising accuracy. All of these data permit us to establish the pattern of the acute radiation syndrome in man. This is an extremely useful point of reference for comparison with much of the animal experimentation that has been done, both here and abroad.

So much has been written about the injuries of the Japanese that we need only review briefly the clinical course of their illness (3). The clinical syndrome of the patients with radiation injuries uncomplicated by thermal burns or other wounds can be divided into four chronological phases. Phase I consisted of prostration, nausea, and vomiting, and sometimes diarrhea, occurring within an hour or so after exposure and persisting for a day or two. Phase II was a period of relative well being, lasting from the time of recovery from Phase I until the development of Phase III. The height of the illness was usually reached during Phase III and was characterized by gradually developing fever, diarrhea, loss of hair, hemorrhages in the skin and internal organs, especially the intestines, and ulceration of the mouth and throat. Those patients who survived this febrile illness entered into Phase IV, a prolonged period of convalescence leading to eventual and apparently complete recovery.

The radiation dose received by the Japanese diminished with increasing distance from the hypocenter. It is estimated that the  $LD_{50}$  occurred at somewhat more than a thousand yards from the point below the explosion. Unfortunately, the flux and the spectrum of the primary and secondary radiations at this distance are not known, and computations are uncertain. The  $LD_{50}$  in man is usually considered to be approximately  $400 \pm 100$  r of  $\gamma$ -rays, and it must be supposed that the radiation dose received by persons near the hypocenter was equivalent to such a dose of  $\gamma$ -radiation. It is known that the radiation at this distance was composed largely of  $\gamma$ -rays, and there is reason to suspect that much of the primary radiation had been degraded into relatively soft secondary rays. The reasons for suspecting the soft component is the prevalence of baldness in the surviving Japanese. The epilating dose of x-rays from a 1 Mev generator applied to the scalp is of the order of 1000 r (depending on the age of the subject and his natural tendency to baldness). This dose of 1 Mev  $\gamma$ -rays, if delivered to the entire body, would almost certainly be fatal to a man. The epilating dose for softer radiation, however, is smaller (375 to 500 r of unfiltered 75 kv. x-rays in children and less for adults). It must be assumed, therefore, that the radiation responsible for the epilation was considerably softer than that of the primary  $\gamma$ -rays given off by the fission reaction and fission fragments.

*Reactor accident victims.*—The injuries which occurred at the Los Alamos Scientific Laboratory as a result of two accidents with critical assemblies varied somewhat from the clinical syndrome described above. The character of the exposures and the nature and types of tissues which were injured account for the variation in the illness suffered under the two situations. These cases, which have been reported in detail by Hempelmann, Lisco & Hoffman (4), differ from the Japanese in three respects. First, the major part of the damage was done by moderately fast neutrons, the average energy of the neutrons escaping from the shielded reactors having been estimated to be below 1 Mev. Secondly, the limited path of neutrons of this energy in tissues (the mean-free path in aqueous tissue being 2.6 cm.) resulted in the most severe damage being done to the superficial layers of flesh nearest the reactors. This means that the body tissues were not as uniformly irradiated throughout as were those of the Japanese. Thirdly, the radiation flux to which different parts of the body were exposed was not uniform in the three most severely injured patients. In the two fatally injured persons, the hands and arms received exceedingly large doses, and the heads and legs received relatively smaller doses.

Before discussing the illness of these patients and how it resembles yet differs from that of the Japanese, it is interesting to consider the radiation. The neutron dose presented a new problem from the point of view of measuring the total energy dissipated in the entire body. Fortunately, measurements of the induced radioactivity of the sodium and phosphorus of the blood serum gave a good index of the neutron flux. Specific activities of serum sodium are given in Table I. Since the specific activity of these elements de-

pended on the total number of neutrons captured in the entire body, these measurements gave data of greater value than those obtained from the induced activity in special materials worn in badges and carried on their person.

Once the neutron flux was computed, it was possible to calculate the energy dissipated in the body tissues by assuming that the average incident neutron energy was below 1 Mev. The energy imparted to the body tissues by the neutrons was derived from the proton recoil of the fast and moderately fast neutrons. The slow-neutron-capture reaction in tissue nitrogen and the  $n,\gamma$  reaction in hydrogen of thermalized neutrons accounted for the remainder of the energy dissipated in the tissues. In addition to the energy from the neutrons, there were  $\gamma$ -rays from the fission reaction and fission

TABLE I  
REACTOR ACCIDENT VICTIMS: DOSES

Case	Serum Sodium Activity*	Average Body Dose†	Incident Dose Equivalent	
			Neutron as‡ Soft x-ray (r)	Gamma Ray (r)
1	18.0	404	840	487
2	1.1	11	45	3.2
3	73.6	709	2036	156
4	13.3	136	407	41
6	7.1	71	210	19
7	3.8	39	100	10

\* Specific activity of  $\text{Na}^{24}$  in disintegrations per second per milligram.

† Dose in 1 Mev gamma rep (roentgen-equivalent-physical).

‡ Based on assumption that the heavy particle dose distribution is approximated by 80 kv. peak x-rays.

fragments. The radiation dose computed for the various neutron reactions and  $\gamma$ -ray sources is shown for six typical cases in Table I, column 3. The heavy particle doses were converted to gamma equivalent dose by the radiobiological effectiveness factor (RBE) of 5.

Expression of the dose in terms of equivalent gamma rep does not take into account the distribution of the dosage in the body. Therefore, the dose has also been expressed in terms of the hard and soft radiation components. The hard component is that attributable to  $\gamma$ -radiation given off from the reactor as well as from the capture of slow neutrons. This hard component is expressed in terms of gamma roentgens. The soft component is that attributable to the proton recoil of the fast neutrons and the  $n,p$  reaction in tissue nitrogen.

Since the dose distribution of the moderately fast neutrons in aqueous tissue approximates that of soft x-rays, the radiation dose attributable to



these heavy particles is expressed in terms of the equivalent roentgens of 80 kv. peak x-rays, using a conversion factor of five to take into account the greater biological effectiveness of the neutrons. The choice of this conversion factor is an arbitrary one and is based on a comparison of the killing effect of fast neutrons and  $\gamma$ -rays in mice. It is undoubtedly low for certain actions of neutrons, particularly those producing late injuries. These doses are given in the last two columns of Table I. It should be pointed out that these are average doses which would have been delivered had the radiation been delivered uniformly over the entire body. Such a uniform radiation flux was not the case in three of the exposed persons. The hands of Case 1 and Case 3 received a much higher dose, the abdomen a somewhat greater dose, and the heads and legs a smaller dose than this average. Case 1 received a soft x-radiation dose of 20,000 to 40,000 r to the right hand and 5000 to 15,000 r to the left hand. Similarly, Case 3 received 3000 to 10,000 r to the right hand and 15,000 to 30,000 r to the left hand. This is based on a guess at how long the hands remained in a region of known radiation flux. Similarly, the head and left arm of Case 3 were exposed to a greater dose of radiation than was the rest of his body.

The illness of the two fatally injured patients was similar to that described for the Japanese. Both patients showed a prompt initial reaction (nausea, vomiting, prostration, and mild fall in blood pressure) during the first exposure day. In Case 1, the more heavily exposed, the initial phase was present in less severe form during the second day. This early reaction was followed by a period during which the patients had few symptoms except for those attributable to the severe injury to their hands. Within a week after exposure, both patients went into the toxic phase of the syndrome, characterized by increasingly high fever, pronounced weight loss, and severe gastrointestinal symptoms. Despite supportive therapy, which consisted largely of the administration of whole blood and plasma, fluids, and penicillin, death occurred in Case 3 on the ninth postoperative day and in Case 1 on the twenty-fourth day after the accident.

Certain aspects of the illnesses of these patients deviated from those seen in the Japanese. The unusual reactions of both patients are believed to be related to the uneven irradiation of the body as well as to the magnitude of the radiation doses delivered to certain parts of the body. Thus, presumably as a result of the intense irradiation of his abdomen, Case 3, the more heavily irradiated of the two fatally injured patients, suffered from severe abdominal distention attributable to paralysis of his alimentary tract. It was necessary for this patient to have his stomach drained continuously by a stomach tube for relief of symptoms. Terminally, this patient showed circulatory collapse (a disturbance of blood flow in the tissues like that seen in shock). Just before death he developed jaundice, and small hemorrhages appeared in his skin and internal organs. The febrile illness of Case 1 developed more gradually and showed complicated side reactions superimposed on the general pattern of the acute radiation syndrome. In addition to mild diarrhea and

abdominal distention, which developed during the second week after exposure, there was a biphasic inflammatory reaction of the membranes of his mouth and throat. This began during the second week of the illness and, after improving briefly, became ulcerative in character during the last few days of his life. The patient also had an attack of rapid heart action (250 beats per minute). This is not believed to be a specific effect of radiation per se, but rather was attributable to aggravation of a heart condition that the patient had for many years. The disturbance of heart rhythm was followed by clinical signs characteristic of an inflammatory process of the outer surface of the heart. This patient died on the twenty-first day after exposure without showing any signs of hemorrhage.

In addition to these constitutional reactions, both patients suffered from the extreme injury of their hands and arms and from the less marked but still severe destruction of the skin of their bodies. The rapid response of the tissues was the result of the overwhelming doses of radiation delivered to these tissues, equivalent to thousands of roentgens of x-rays. Swelling of the subcutaneous tissues and changes in the blood flow of the hands and fingers were noted within a matter of minutes in Case 1 and hours in Case 3. This inflammatory reaction progressed until there was destruction of the skin with the formation of large blisters on the hands of Case 1 within three days after exposure. By the time of death, all of the skin of this patient's hands and forearms sloughed off. The denuded tissues of the fingers became gangrenous and shriveled at the time of death. The abdomen of this patient was also blistered and the hair of the scalp and beard was lost. In Case 3 the progress of the radiation reaction in the hands and arms was stopped by packing the upper extremities in cracked ice. This was, in effect, equivalent to amputating his upper extremities. This patient also showed a severe reaction of the skin of his abdomen, but this had not reached the blistering stage at the time of death.

Of the eight survivors, only two had symptoms characteristic of the acute radiation syndrome. Case 4 showed an initial reaction, chiefly nausea and vomiting of moderate degree. He was asymptomatic during the two-week period of hospitalization following the accident except for a brief bout of fever and prostration at the end of the first week. Beginning the third postexposure week, he lost some of the hair of his scalp and beard and found that he was very weak on exertion. The extreme weakness, which lasted about three months, was in striking contrast to his apparently normal strength when he left the hospital. There was evidence of severe damage to the germinal tissues, developing within a matter of months following exposure, but this proved to be of a temporary nature. Five years after exposure, the patient is in good health, although he has developed radiation cataracts in both eyes which interfere somewhat with his vision. He has become the father of a healthy, normal child.

Six of the remaining exposed persons showed no symptoms of any kind,

even though the radiation dose of several was equivalent to 50 to 100 r of soft x-rays.

The blood counts of the more heavily irradiated patients showed pronounced changes. There was a marked increase in the total white count of the fatally injured persons lasting several days. This was probably related to the injury of their hands and arms. In both patients, the lymphocyte count dropped promptly, as it did in most of the survivors. Terminally, the blood count and the platelets of the fatally injured patients fell to an extremely low level. The clotting time of the blood of the heavily irradiated patients was increased; at the time of death, the blood of Case 3 was unable to coagulate when allowed to stand in a test tube for 24 hr.

Of the other laboratory studies done on these patients, the only findings of interest indicated: (a) a moderate change in the electrolyte and nitrogen levels of the blood of Case 3 and an increase in the globulin fraction of plasma protein; (b) an increased urinary excretion of the amino acids amounting to several grams per day; and (c) induced radioactivity of the blood and urine sodium and phosphorus. The highest activity was found in the urinary phosphorus of Case 3, amounting to 357 disintegrations per second per milligram of phosphorus at zero time.

*$\beta$ -ray burns—Eniwetok.*—In contrast to the illness produced by exposure of the entire body to a single dose of ionizing radiation, that which occurs when a small portion of the body is overexposed is much less severe. This is illustrated by the case histories of the four persons who received  $\beta$ -ray burns at the 1948 Eniwetok tests (5). These exposures resulted from hand contact with fission fragments which were much more strongly radioactive than was realized at the time. There is no way to compute the actual dosages delivered to the injured tissues, but the maximum dose of  $\beta$ -radiation was estimated to be 3000 to 16,000 rep (93 ergs per gm.) at the surface of the skin. The  $\gamma$ -radiation from the fission fragments added perhaps 100 r to the hand dose. The highest body dose measured by a film badge worn on the chest was 17 r.

An important practical fact emerging from these accidents is the itching and burning of the skin noted during the exposure. One of the persons changed his rubber gloves several times because he believed they contained some irritating chemical.

The symptoms which varied in severity for each patient were referable almost entirely to the hands. They consisted of swelling of the fingers, beginning several hours after exposure, and blistering starting after one week and reaching a peak four weeks after exposure. Pain was the only symptom experienced even during the height of the reaction. There was a slight elevation of each patient's temperature and an increase in his white blood cell count. Healing of the skin began during the second month. In one patient, the subcutaneous tissues of the index finger of the right hand sloughed, forming an ulcer which exposed the tendons of the finger. Since it was evident that healing would be slow and probably incomplete, the injured skin and some sub-

cutaneous tissue was removed surgically. New skin, taken from the abdomen, was transplanted to the fingers. This was accomplished by a series of five consecutive operations. Almost five years later, the most seriously injured finger is stiff and atrophied, but the skin is in good condition. In two other patients, the wounds were completely covered by thin, fragile skin within a period of four months. Since this new skin was delicate and vulnerable to injury, it and the scarred subcutaneous tissues were replaced surgically by healthy skin from another part of the body. This was successfully accomplished in these two patients. The fingers of all persons (although some of them are slightly atrophied or slightly stiff) are in good condition five years after the accident.

*Acute thorium poisoning.*—Unlike the many injuries in man which have been produced by exposure to ionizing radiation originating from sources outside the body, there is only one reported case of acute radiation injury attributable to internally deposited radioactive material (6). This occurred when a 26 yr. old girl committed suicide by swallowing a solution of Thorium X. The total amount of radioactivity ingested was equivalent to 14.5 mc. of radium, but much of this was lost when the patient vomited twice shortly after drinking the solution. The patient gradually developed fever and died fifteen days after ingesting the radioactive material. Death was attributed to destruction of the blood-forming tissues and the alimentary tract. Initially, there was a marked rise in the white blood cell count and then a gradual fall until, during the last few days of life, there were only 20 to 300 cells per c.mm. of blood.

#### EXPERIMENTAL THERAPY OF ACUTE RADIATION INJURY IN ANIMALS

*Blood transfusions.*—Intensive investigation has been conducted in several laboratories during the past two years to determine the value of blood transfusions on the mortality rate of irradiated dogs. Two preliminary reports suggest that procedures which replace circulating blood of an irradiated animal with fresh blood taken from a nonirradiated animal increase the survival rate of dogs given lethal doses of radiation. The experiments of Salisbury *et al.* (7) and of Swisher & Furth (8) employ somewhat different transfusion techniques but show essentially the same results. In both experiments, the number of animals used is small and the benefit not great. However, if these experiments can be confirmed on larger groups of animals, this technique will provide a method of treatment for use in the occasional case of accidental radiation injuries. The technical difficulties of this type of treatment would prevent its being used on more than a few persons at a time.

Allen (9) at the Argonne Laboratory in Chicago and Furth and associates (10) have studied the effect of blood transfusions used in the conventional manner on the illness and mortality of irradiated dogs. Allen reports that repeated transfusions of fresh blood to dogs exposed to doses of radiation in the sublethal and lower-lethal range are not beneficial. These experiments have been confirmed by Furth, who used blood stored for several days under

conditions which prevail in a blood bank. In both experiments, the transfusions were given either at a predetermined schedule, e.g., three times weekly, or when the red blood cell count fell slightly below normal. The data obtained by both investigators indicate that, at least in dogs, transfusions of fresh or stored blood have no value as long as the red blood cell count is normal or slightly below normal. The experimenters do suggest that transfusions are ineffective if used to replace blood lost from other causes. Indeed, in the case of extreme blood loss, it is the impression of some investigators that the transfusions at the height of an animal's illness may tide him over a critical period, following which spontaneous recovery occurs. The experiments of Jackson and associates (11) indicate that transfusions of platelets, freshly separated from blood, stop the bleeding that occurs at the height of the illness. Platelet transfusions do not prolong life or reduce the mortality of irradiated dogs.

In the course of experiments on transfusions, Furth (10) observed that the prophylactic use of aureomycin daily after irradiation does not benefit irradiated dogs. This is in contradiction with earlier work which reported that aureomycin was effective in reducing mortality of rats and dogs. The experimental data indicate that in clinical practice the use of blood and aureomycin must be left up to the judgment of the physician in charge. The logical conclusion is that blood should be used only as replacement therapy and that the broad-spectrum antibiotics should be used at the discretion of the attending physician, especially if other injuries have been sustained.

*Mobilization of heavy elements.*—Other experimental work which is of use to the clinician confronted with the problem of treating radiation injuries centers about the action of chelating agents in removing heavy metals from the body. The chelating agent which has been most extensively studied is calcium ethylenediaminetetra acetate (CaEDTA) [(12) Report of a Conference held at the Massachusetts General Hospital]. The use of this complexing agent does not constitute treatment of a radiation injury in the strict meaning of the word, as its effectiveness is based on the prevention of radiation injury by removal of radioactive materials before they can produce radiation damage. CaEDTA has been found to be effective in mobilizing plutonium as well as yttrium, americium, and lead, even after they have been deposited in the bone. It is most valuable in removing metals if administered shortly after the element has been introduced into the body. It will increase the excretion rate of the radioactive elements several days after they had been administered.

*Aloe vera ointment.*—An ointment extracted from the plant, aloe vera, has been found to promote the healing of  $\beta$ -ray burns in rabbits (13). It had been used clinically several years ago for treatment of acute skin reactions in patients subjected to radiation therapy. This experimental confirmation of clinical observations suggests that the material may be of value in treating superficial radiation injuries.

*Tissue fractions promoting recovery.*—In addition to the direct clinical



work, there are current fundamental investigations which may ultimately lead to improved methods of treatment. The recent investigations on the role of the spleen and biological materials taken from the spleen and other tissues on radiation injury have been reviewed by Jacobson (14). The practical value of these experiments is that they offer hope that it may be possible to develop a specific form of therapy which can be used in the treatment of radiation injuries after their occurrence. This is in contrast to the supportive therapy which corrects the disturbed physiology of the body resulting from the injury of selected tissues. Thus, replacement of blood, fluid, and electrolytes, and the use of antibiotics to prevent or counteract infection measures are directed at the treatment of events which are strictly secondary to the radiation damage.

Interest in the spleen was aroused by Jacobson's (14) early experiments which showed that shielding the spleen from the incident rays raised the lethal dose of radiation for mice by a factor of two. Transplantation of spleens of nonirradiated animals was also beneficial as was the injection of bone marrow, spleen homogenate, and embryonic tissue extracts. In all of the work of Jacobson, it has been emphasized that the tissue extracts used were not cell free. Nevertheless, Jacobson believes that the effective agent is a cell-free factor which is mediated through the blood stream. He points out that his experiments have not proved this. This position is supported by the recent experiments of Cole, Fishler & Bond (15), who find that the administration of spleen homogenates and preparations of spleen cell nuclei benefit the irradiated animal. These tissue preparations are composed mainly of cell fragments, but it has not been ascertained that they are cell free. There still remains the possibility that the beneficial effect of the tissue fractions is attributable to a seeding of intact cells which are blood forming and proliferative [Kaplan (16) and Storer *et al.* (17)].

*Chemical modification of cell sensitivity.*—Of theoretical interest are the experiments which deal with the modification of radiation damage by means of pretreatment with chemicals. Cysteine, thiouria, glutathione, para-aminopropiophenone (PAPP) are among an ever-increasing number of the protective chemicals [Patt (18)]. Rendering an animal anoxic also affords radiation protection.

*Hormonal effects.*—Administration of estrogen before the radiation dose is found to reduce the mortality in animals (19). The steroid hormones, cortisone and desoxycorticosterone acetate (DOCA), have been shown by Mirand, Reinhard & Goltz (20) to have pronounced ability to reduce mortality in mice when given immediately before or after irradiation. The apparently conflicting reports on the protective effect of cortisone are attributable to toxicity arising from heavy dosage at a rate greater than 1 mg. per day for mice. Experiments on different mouse strains point to wide differences in response to the protective action of the steroid hormones (22) as well as in the results of shielding the spleen (21) and the head (22) of the animal. These



differences mean that in humans a wide range in degree of response is to be expected.

#### LATE RADIATION EFFECTS IN MAN

In the preceding sections the immediate symptoms of acute radiation disease were described. Typical of the majority of health hazards of diverse kinds, acute conditions occur only in accidents which are relatively rare. In the following section a description is given of long-range effects of radiation which are a consequence of low as well as high radiation doses and which may be likened to the long-range effects of chronic poisoning or other common hazards of modern life.

The term "late radiation effects" is used in this chapter to designate all undesirable biological results of radiation exposure appearing long after the dose is received. The latter may vary from a single large dose to a low dose spread over a long period of time. Skin cancer of the hands of the early radiologists was among the first of the unsuspected late effects of radiation exposure to develop. The first case was reported in 1902 (23); and, by 1907 (24), seven cases had been published in the medical literature. Many cases of skin cancer were observed in the years immediately following. Hesse (25) mentioned 94 cases in an article published in 1911. In the same year (26), the first death of a radiation worker from leukemia was recorded; and, in 1914 (27), a well-known radiologist died as a result of aplastic anemia. Other forms of the delayed reactions that have occurred in man are cancer of the internal organs, cataracts, and developmental abnormalities. The last of these late effects occurs in children who were exposed in utero or after birth to a large dose of ionizing radiation. Sterility of either the male or female may also result from localized exposure of the germinal tissues. Experience with irradiation of lower animal life also suggests that shortening of life (by causes other than cancer) and genetic mutations in germ plasm transmittable to one's offspring may also result from exposure of human beings to ionizing radiation.<sup>2</sup>

The delayed effects of radiation usually develop many years or, at the earliest, several years after exposure to a single large dose of ionizing radiation or after repeated or protracted exposure. Cataracts in adults or developmental abnormalities in children are an indirect result of lethal injury to cells which are able to survive for some time after exposure. As a result of the death of the slowly proliferating epithelial cells of the lens epithelium, there is a gradual degeneration of lens substance. The malformation of children exposed either before or after birth is a natural sequel to tissue injury sus-

<sup>2</sup> Aplastic anemia, a disease caused by destruction of the blood-forming tissues, is not considered in this section. It is a well-established late effect of repeated gross overexposure of the body to ionizing radiation. Since it is not a likely result of a single accidental exposure or of protracted exposures under the existing working conditions, it should not concern persons working in the nuclear science fields.

tained at a critical period of rapid growth and development. Interference with proper organ development leads to malformation, whether the injurious agent is ionizing radiation, a virus infection of the mother, malnutrition, metal poisoning, or other toxic states in the embryo.

In contrast to these late effects of radiation exposure, leukemia, cancer, and genetic mutations in germ cells presumably are attributable to nonfatal injuries of irradiated cells. If the modification of the chromosomal material is not severe enough to cause death during a subsequent division, the damaged cell can divide and produce viable but somewhat abnormal daughter cells which may be viable mutants. A mutation may occur in a germ cell, in which case the mutant genes can be passed on to the offspring. If, on the other hand, the mutation occurs in body cells (other than germ cell), the altered characteristics will be transferred to the descendants of the mutant cells, whatever the tissue. In this sense, cancer or leukemia may be considered to be a "somatic mutation," although this cannot be proved strictly according to genetic methods. A somatic mutation is probably not a simple affair, but it is the result of one to four distinct genetic events occurring in a single cell (28, 29). Mutations in germ plasma, although they have not been identified in man, should not differ in nature from those that occur spontaneously (one in  $10^5$  births) (2, chap. 22). At least this has been the experience in *Drosophila* and in other lower animals.

The delayed effects of radiation are not unique or specific. Moreover, similar reactions occur spontaneously in uninjured tissues. Thus, cancer of the skin may occur in undamaged skin or in the scar of a thermal burn (30). Bone malignancies also appear without known cause or in patients with Paget's disease, an unusual disease of the bone (31). Radiation cataracts are similar to, but differ in some respects from, those that appear in older non-exposed individuals.

Leukemia was once considered to be a rare disease and still receives publicity because of its supposed rarity. Its incidence has been increasing in this country since 1900 and has risen sharply since 1920 (32). In 1940, it was reported as the cause of death of 3.62 of every thousand deaths of all causes. Leukemia is a malignant disease of the blood-forming tissues resulting from the uncontrolled growth of any of the cell types constituting these tissues. The lymphocytes or granulocytes are the most commonly involved. Their rapid multiplication has three major consequences: (a) a crowding out of other normal cell types in the bone marrow, thereby causing anemia and a bleeding tendency; (b) a flooding of the blood stream with abnormal white blood cells, sometimes numbering more than one million cells per cubic millimeter of blood (one hundred times the normal); and (c) the enlargement of the lymph nodes and spleen, often to a marked degree. The disease may take one of two forms. The acute type, which is usually found in children or young adults, is a rapidly fatal disease lasting a matter of months or, at the most, a year or two. Treatment with certain drugs, e.g., aminopterin, is often quite effective temporarily. Chronic leukemia, by far the more frequent,

is usually found in persons over 45. This disease lasts for years and responds well to treatment with x-rays,  $P^{32}$ , or the radiomimetic drugs, such as the nitrogen mustards.

The fact that late manifestations appear so long after irradiation makes it difficult to assess the hazards of exposure. A latent interval of 25 or 30 years is not uncommon, for example, in radiation-induced cancer. The long interval between exposure and the ultimate effect make a causal relationship conjectural. Another complicating aspect of delayed reactions is that the diseases which are characteristic of the late effects of radiation also occur as part of the normal aging process. It is difficult to decide, therefore, except by the study of large populations, whether or not the incidence of the illness in persons exposed to radiation is increased over that seen in the general population.

Yet, in spite of the long latency and the general technical problems, a study of certain groups of persons who have been exposed to radiation provides data which are useful in assessing the risk of radiation exposure under different conditions. Most valuable information has come from the study of the following groups: the Japanese exposed to the nuclear explosions, radiologists who have worked with x-rays over a long period of time, cyclotron workers irradiated by neutrons, patients treated with x-rays or radioactive materials, early radium dial painters, and miners in Central European mines.

Following is a presentation of specific examples of reactions and, where known, the radiation doses responsible for them. The effects will be discussed according to disease rather than according to the method of exposure.

*Leukemia.*—The incidence of leukemia is reported to be higher than normal both in the Japanese exposed to the radiations from the nuclear explosions as well as in radiologists. Even physicians, who as a group have more exposure to x-rays than most occupational groups, are said to develop leukemia more frequently than the general population. In a recent report from the Atomic Bombing Casualty Commission covering a three year study from 1947 to 1950, Folley, Borges & Yamawaki (33) state that 29 proved cases of leukemia have been found in the persons who survived the explosions at Hiroshima and Nagasaki. Twenty-two of these cases occurred among the 39,257 people who were within 2000 yards of the hypocenter at the time of detonation. Seven cases were observed in the remainder of the population (155,970) outside the 200 yard circle. Further breakdown of the data shows that four cases of leukemia developed in the 2071 surviving persons who were within the 1000 yard circle and who, therefore, presumably received an  $LD_{50}$  dose of radiation or more. All of these persons lost their scalp hair soon after exposure. Twelve cases of leukemia developed in survivors who were from 1000 to 1499 yards of the hypocenter, and six cases appeared in the 23,363 individuals who were in the 1500 to 2000 yard zone. Seventy per cent of the last two groups were epilated after exposure. Expressed in another way, the leukemia incidence per million living persons is 458 for individuals

inside the 2000 yard circle and 32 for persons outside this zone. The latter value is not increased over the normal incidence in the Japanese population (30 per million living people). The difference in the incidence of the disease in the two exposure groups is significant, even if calculated on the basis of total exposed population including the large percentage killed within the 2000 yard zone. In all except one exposed Japanese subject, the leukemia was of the acute type. Eighty-six per cent of the cases occurred in persons 45 yr. old or younger.

As in the case of the acutely exposed Japanese, the number of cases of leukemia occurring in chronically exposed radiologists is small; but the increase in the incidence of the disease seems to be highly significant. Understandably, there are no good data about the doses of radiation sustained. Scattered reports of leukemia occurring in x-ray and radium workers have appeared in the literature since 1911, but Henshaw & Hawkins (34) were the first to attempt a systematic investigation of the subject. They analyzed the obituary notices (about three-quarters of which give the cause of death) in the *Journal of the American Medical Association* and found that the percentage of deaths among physicians attributable to leukemia was 5.3 per thousand deaths from all causes. This is 1.6 times the incidence given for the general adult male population in 1940.

Peller & Pick (35) have analyzed the deaths of physicians according to age groups. They found that the increase in leukemia in physicians over that seen in the general male population is especially marked in the younger age groups, 25 to 40 yr. It was almost seven times the normal incidence in the physicians who died between the ages of 25 and 29. The ratio diminishes to two to three times normal in the 40 to 70 yr. age group. Unlike leukemia, the incidence of other forms of malignancy among doctors is lower than that of the general male population of the same age group. This relatively low incidence of cancer in physicians has also been noted by Dublin & Spiegelmann (36).

March (37, 38) found 23 reports in the medical literature of deaths of radiologists from leukemia since 1911. He added 14 new cases which he obtained from the obituary notices of 299 radiologists who died in the 20 yr. period, 1928 to 1948. Death from leukemia occurred in this group at a mean age of 58.8 years. During the same period, there were 334 deaths among 65,992 physicians who were not recognized radiologists. Thus, the death rate from leukemia in radiologists was nine times greater than that in the other physicians dying during the same period of time. It must be pointed out that, in addition to radiologists, many physicians in general practice or in specialties also use x-ray equipment. Ulrich (39) reports 2 deaths from leukemia in a group of 60 skin specialists who died between 1935 and 1944. Peller & Peck (35) report that the leukemia death rate even in nonradiologists and nondermatologists is 1.2 per cent in the 35 to 70 age group. This is twice the incidence seen in the general male population.

Leukemia thus occurs at a significantly higher rate in persons exposed to

a large single dose of total body ionizing radiation or to repeated doses over a long period of time. In the case of the Japanese with leukemia, the radiation doses were high, as is indicated by the baldness of almost all patients. Even though the incidence of leukemia may increase in time, it should be pointed out that the probability of any given individual exposed to a large dose of radiation developing leukemia is not great. Thus, only 1 in 500 in the group surviving an LD<sub>50</sub> or more developed leukemia during the study period.

The exposure data for the physicians who developed leukemia is extremely poor, but it is probable that the exposures were high when compared with the present-day acceptable levels for repeated exposures (300 milliroentgens per week). In the 1920's, radiologists were careless in exposing their hands and bodies, particularly when using the fluoroscopes which were poorly shielded in the early days of radiology. Even now, the dose rate of a medical fluoroscope is 0.03 to 0.07 r per minute on the fluorescent screen. Twenty-five years ago, when the phosphor screens were inefficient, the radiation output of the machine was, of necessity, much higher. The association of leukemia and radiation exposure in the Japanese and in the radiologists is not rigorously one of cause and effect; nevertheless, this seems a highly probable association, especially in view of similar findings in irradiated animals. (See the chapter by Furth & Upton, page 303.)

*Cancer.*—In contrast to the leukemic type of malignancy which is distributed generally throughout the blood-forming tissues and which is produced by total body exposure, radiation-induced cancers arising in individual organs appear to be the result of the gross overexposure of a localized region of the body.

The development of cancer in irradiated skin has been thoroughly reviewed by Hueper (40) and Lacassagne (41). Such cancers characteristically appear in skin which has been injured by acute exposure to radiation or by protracted or repeated exposure over a long period of time. Tumors may arise in the regenerating skin at the edge of a persistent radiation ulcer, but of greater interest to the radiation worker is the kind that develops in skin showing chronic radiation damage (atrophy of the skin and underlying tissues and localized areas of tissue overgrowth). Cancer in chronically damaged skin is usually multiple, several small tumors arising in nearby areas of skin. It is generally accepted that cancers develop only in skin which is grossly damaged. The latent period between the exposure and the development of the cancer is reported to be from four to twelve years (41).

Despite the hundreds of cases of skin cancer which have occurred, the dose of radiation which, if delivered as a single exposure, or as several exposures in the period of a few months, will prove to be carcinogenic, is not known. The acute carcinogenic dose must be at least several thousand roentgens. In order to produce severe late skin changes, the exposures must exceed those used in radiation therapy, 4000 r of 220 kv. x-rays given at a rate of 200 r per day being an example of the dosage used in therapy. The car-



cinogenic dose of radiation delivered daily over a long period of time is not known either, but Parker (42) reports that changes have occurred in the skin of persons whose hands were exposed to 4 r of  $\gamma$ -rays per day.

With the use of more penetrating radiations in medicine, cancers of tissues below the skin have been reported with increasing frequency in the past 20 yr. Wilson & Brunschwig (43), in 1939, reported on 25 cases of sarcoma of the subcutaneous tissue which they had collected from the medical literature and one case of their own. The tumors developed 3 to 24 years after treatment of these patients with x-rays for various diseases of the skin and bone. Goolden (44) found five reports in the medical literature of cancer of the throat and one cancer of the thyroid arising after intense irradiation of these regions. To this list he added four more cases of cancer of the throat in patients who had received heavy x-ray treatment of the neck. The latent interval in his cases was from 26 to 30 yr. The radiation dosage in these cases is not known, but must have been high, at least in three of the cases, which showed severe late damage in the overlying skin.

Good data about carcinogenic radiation dosage in an internally situated tissue is found in the case of some tumors arising in irradiated bone. Hatcher (45), in 1945, reported twenty-four cases of osteogenic sarcoma collected from the literature. Six of these patients had received radium and the rest x-ray treatment. To this list he added three more cases which developed bone tumors 4 to 12 yr. after treatment. Cahan and associates (46) reported a series of bone tumors developing in irradiated patients studied at the Memorial Hospital in New York City. Computations of the doses delivered to the tissues which later became malignant showed a range from 1500 r to 9000 r. The latent period in this group of patients was from 3 to 21 yr. A feature of these doses is that the energy absorbed by bone from x-rays in the range of 100 to 140 kv. peak is much greater than is that absorbed by aqueous tissue. Stenstrom & Marvin (47) found that energy absorbed from a given radiation flux may be four times as great in bone as in soft tissue. It should be emphasized that the actual number of proved cases of radiation-induced cancers is very small compared to the large numbers of patients treated daily with x-rays.

Perhaps our most accurate information about the radiation dosage required for the production of tumors comes from the study of persons who have stored long-lived radioactive materials in their bodies for many years. Extensive studies of the late effects of internally deposited radioactive materials have been made on luminous dial painters as well as on patients given radium many years ago. A series of 30 patients containing varying amounts of radium for the past 25 yr. or so has been reported recently by Aub *et al.* (48). Fifty more radium-containing patients are being studied currently by investigators at the Argonne National Laboratory (49). The first group of patients consists of persons who came to Dr. Aub and Dr. Martland because of illness caused, in part, by the radium. Most of these patients were exposed to radium at least 25 yr. ago. The second group



of patients was unselected as far as symptoms were concerned. The Argonne investigators were able to find lists of patients who had been given radium and studied these persons regardless of whether or not they were ill. One of the most interesting facts to come out of these studies is that a large number of persons was given radium for medical reasons in the 1920's. It was an accepted tonic and was used in the treatment of rheumatism. Radium nostrums were prescribed by many qualified physicians who were then unaware of its toxicity. It has been estimated that many thousands of persons must have received radium nostrums for one reason or another. Such practices came to an end, of course, when the toxicity of radium was established in the late 1920's. In some medical centers of questionable reputations, the administration of radium has continued up to the present day.

The information gained from the study of the Boston and Chicago series of patients may be summarized as follows. Radium taken orally or by injection is deposited in the bones and, to a lesser extent, in the soft tissues of the body. Most of the radium is excreted promptly, but a small fraction remains fixed in the bones throughout the life of the person. This is also true in the case of mesothorium, the 6.7 yr. radium isotope to which many dial painters were once exposed.<sup>3</sup> Eleven of the 80 patients have developed malignant tumors. Most of the tumors arose in the bone, but some have developed in the sinuses of the nose. Two patients containing 0.5 and 0.8  $\mu\text{g}$ . of radium respectively in their skeletal systems developed malignant bone tumors. The largest amount of radium found in any of the patients with tumors was 8  $\mu\text{g}$ . In contrast to these patients who developed tumors, other persons in the series have lived for many years without developing tumors, despite 10 to 20  $\mu\text{g}$ . of radium fixed in their bones.

Assuming that the radium is uniformly distributed throughout the bones, it can be calculated that the radiation dose of  $\alpha$ -rays in the bone is 0.11 rep per day. The radiation dosage in the many "hot spots" distributed throughout the bone is estimated to be at least ten to fourteen times the average dose delivered to the bone. Thus, small discrete regions of bone in persons containing 0.5 to 1.0  $\mu\text{g}$ . received at least 0.5 to 1.0 rep per day of  $\alpha$ -radiation. Multiplying this rate by a conversion factor of ten, to account for the biological effectiveness of the  $\alpha$ -particles, the bone tissue in the hot spots of these persons must receive the equivalent of 5 to 10 r of x-rays per day (rem). This is the dose delivered 25 years after exposure. The initial dose rate during the first few months or years, especially in the patients containing mesothorium, was much higher.

Another example, of a malignant tumor in which ionizing radiation is suspected, is the lung cancer found in the miners who work in the mines of

<sup>3</sup> The high mesothorium content of the luminous dial paint often used before 1926 has not been considered in the recent writing on radium toxicity. In his extensive discussion of this subject, Evans points out that the luminous dial paint used in some plants consisted of commercially pure mesothorium which contained 20 per cent radium as an impurity.

Saxony and Czechoslovakia. This controversial subject has been thoroughly reviewed by Hueper (40) and the Lorenz (50). [Also, see Evans (51, 52) and Bale (53)].

One final example of cancer produced by radiation is the liver cancer produced by thorium oxide. Colloidal solutions of this substance were used in medicine in the early 1930's under the name of Thorotrast. When injected intravenously, the colloidal particles were taken up by the liver and spleen. This property, combined with its radio-opacity, was used to outline these organs in roentgenograms of patients who were suspected of having disease in these organs. One case of cancer of the liver has been reported in a woman who received this material 12 yr. before (54). Other patients are being studied currently.

Before concluding this discussion of radiation-induced tumors, it must be pointed out that there are many factors besides radiation which are concerned with the developments of tumors. Thus, in animals, it has been shown that administration of carcinogenic materials (55) or certain hormones (56, 57) has a profound effect on the ability of radiation to produce tumors. Also, there is an innate susceptibility of individuals to tumor formation; an example of this is found in the case of a 5 yr. old girl who developed multiple cancers in an area of skin subjected to irradiation shortly after birth (58). X-rays were given as treatment for an enlarged thymus shortly after this child was born. Presumably, several doses amounting to 100 to 200 r were administered to her chest. It is undoubtedly true that this child would have developed tumors spontaneously or as a result of sunburn or other mild stimulation had she not been exposed to x-rays.

*Radiation cataracts.*—Since 1948, it has become increasingly clear that cataract formation in the lens of the human eye is a phenomenon requiring careful consideration in the protection of radiation workers. In 1949, Abelson & Kruger (59) published a list of 10 cases of cyclotron workers in whom cataracts had been induced by neutrons. The estimated doses varied from 10 to 135 *n* units sustained in time intervals ranging from 10 to 250 weeks. In the same year, Cogan, Martin & Kimura (60) reported 10 cases of cataracts in Japan, 9 at Hiroshima, and 1 at Nagasaki who had been within two thousand feet of the hypocenter of the atomic bomb detonations. Since then, over 200 cases of lens disturbance in the atom-bombed cities have been recorded, the latest observer being Sinskey (61).

Reviews of the subject of radiation cataracts are found in Desjardins (62) and Ham (61).

The minimal acute dose required for the production of cataracts by therapeutic x-rays is in the range of 500 to 800 r. Donaldson (61), quoting Cogan's survey of cases at the Massachusetts General Hospital, corroborates the higher figure. Patients who had received therapeutic x-ray doses of the order of 800 r to the eye as a result of head treatments in the vicinity of the eye showed cataract history. Ham (61), after reviewing the literature,

estimated that 500 r are potentially dangerous from the standpoint of cataract formation. The threshold dose for  $\gamma$ -rays is about 1000 r [Cogan (63)].

Neutrons appear to have greater cataractogenic properties than do x-rays or  $\gamma$ -rays. The first cases to come to the attention of medical workers were those of the cyclotron workers mentioned above. The presence of fast neutrons was recognized as the primary cause of cataract formation, because experience had indicated that sufficiently high doses of electromagnetic radiations could not have been available.

The magnitude of cataractogenic dose of fast neutrons in man can be estimated from the information available on the accidental nuclear reactor victims at Los Alamos. The cases are referred to in the first section of this chapter, in the discussion of acute radiation symptoms (4). As described there, the assessment of fast neutron doses was based upon the measured radioactivity of  $\text{Na}^{24}$  and  $\text{P}^{32}$  found in the blood serum of the victims.

In the reactor accident series, Case 4, age 34, provides pertinent information on fast neutron cataractogenesis. The left side of his head, which showed pronounced epilation, received about 45 rep; the right side, which was turned away from the source of radiation, must have received considerably less, inasmuch as no epilation was manifest. About 28 months after the accident, examination failed to disclose lens damage. However, 4 months later, the left eye showed haziness in the posterior cortex which developed into advanced cataract in the following 6 months. At 58 months after exposure, the right eye showed a definite opacity.

Two other victims near the source of radiation in the accidents, ages 54 and 21, received estimated doses of 21 and 15 rep of fast neutrons respectively to the eyes. They had normal lenses three years after exposure. The estimates are, then, that the fast neutron acute dose for the production of cataracts lies in the range between 15 and 45 rep. Since the right eye of Case 4 ultimately developed cataract and probably was not directly exposed to the source, it may be inferred that the dose of 45 rep is high and not necessarily minimal. Of especial note is the long latent period found in Case 4, namely, 5 yr. for the right eye. Of the 10 individuals exposed, 2 had been touching the source of radiation. Case 1 died in 24 days, having received about 55 rep to the eyes; and Case 3 died in 9 days, having received about 225 rep to the eyes. The short time intervals did not permit a study of lens damage before death intervened.

*Effect on reproductive organs.*—The well-known late effects of irradiation of the reproductive organs are sterility and genetic changes in the germ cells. Sterility is the result of the permanent destruction of the gonadal tissues which produce mature sperm and ova. The marked radiosensitivity of these tissues was first observed in the course of animal studies in 1912 (64). Two years later, when a radiologist died of aplastic anemia caused by overexposure, it was observed that the testes of the radiologist were small and

atrophied (27). Although radiation has been used in medicine for some time as a method of producing sterility, there is no reliable information about the amount of radiation given as a single dose or in a few repeated doses which will cause permanent sterility.

It has been estimated that the male will be permanently sterilized when the testes have been exposed to 400 r in a single dose (64). The sterilizing dose in the female often used by radiation therapists is 600 r, given at a rate of 200 r per day (65). Recent studies of the Japanese have not indicated a decreased fertility. Case 4 of the reactor victims received an estimated 25 rep of moderately fast neutrons. He showed evidence of temporary damage on the germinal tissue but subsequently became the father of a healthy child. Nothing is known about the amount of radiation which, when given repeatedly for many years, will cause sterility. Radiologists as a group do not have a higher incidence of infertility than the general male population. It should be noted, however, that inability to produce children is not uncommon in the male.

Concerning the genetic effects of radiation in man, we must rely entirely on calculations derived on the basis of data obtained from animal experimentation. Bugher (66) states that, of the fifty thousand Japanese babies examined in Japan, those of parents showing evidence of radiation injury have an incidence of abnormalities amounting to 1.4 per ten thousand births, in contrast to the 1.18 incidence in babies of normal parents. No conclusions can be drawn from these data. Families of radiologists do not show a greater than normal incidence of miscarriages, stillbirths, or congenital abnormalities. In this connection, it should be pointed out that the incidence of congenital abnormalities occurring in the normal, unexposed population is higher than is often realized. A 14 yr. survey of Chicago children by Bundesen and associates (67) showed 3.4 congenital malformations per thousand live births.

*Effects on growth and development.*—Radiation is only one of the many injurious effects which will interfere with growth and development of the embryo or with the growing child. There are excellent animal data which show that exposure at certain times of embryonic life interferes with the development of different organs (68). The only studies which have been reported in human beings are of cases which occurred at Hiroshima and Nagasaki. Plummer (69) studied children in these cities who were exposed to the nuclear detonations during the first 20 weeks of gestation. He reports a group of 28 abnormal children among 205 who were exposed in utero. Six are microcephalic and mentally retarded, two show the syndrome known as Mongolianism, and four have congenital dislocation of the hips. All of the cases of microcephaly were within twelve hundred meters of the hypocenter. The only other report to come from Japan is a statement by Bugher (66) that children who were exposed at an early age now show maldevelopment of the teeth attributable to injury of the tooth roots at the time of the bomb detonations.

## GENERAL SUMMARY

The reactions of the human body to acute radiation injury are similar to those elicited by other recognized occupational hazards such as fire, chemicals, and physical trauma. Perhaps the unique feature of radiation injury is the lack of pain or sensation at the moment of occurrence, although it is noted that very intense  $\beta$ -ray exposures were accompanied by itching or tingling of the skin in the Eniwetok cases.

Animal experimentation has promise of possible means for alleviation of the effects of acute radiation injury. The supportive use of steroid hormones or the use of certain tissue extracts may possibly help in the therapy of whole body radiation damage.

Delayed or late effects present the most insidious aspect of radiation injury, although, in this respect, again, the general problem is essentially that which occurs in standard occupational hazards. Moreover, some late effects are comparable to the sequelae of certain diseases, particularly those arising from virus infection.

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